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(71) Applicant *(for all designated States except US)*: HUMAN GENOME SCIENCES, INC. [US/US]; 9410 Key West Avenue, Rockville, MD 20850 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: FENG, Ping [CN/US]; 4 Relda Court, Gaithersburg, MD 20878 (US). ROSEN, Craig, A. [US/US]; 22400 Rolling Hill Road, Laytonsville, MD 20882 (US). RUBEN, Steven, M. [US/US]; 18528 Heritage Hills Drive, Olney, MD 20832 (US). NI, Jian [CN/US]; 5502 Manorfield Road, Rockville, MD 20853 (US). WEI, Ying-Fei [CN/US]; 1714-C Marina Court, San Mateo, CA 94403 (US). SOPPET, Daniel, R. [US/US]; 15050 Stillfield Place, Centreville, VA 22020 (US). MOORE, Paul, A. [GB/US]; 19005 Leatherbark Drive, Germantown, MD 20874 (US). KAYW, Hla [MM/US]; 520 Sugarbush Circle, Frederick, MD 21703 (US). LAFLEUR, David, W. [US/US]; 3142 Quesada Street, N.W., Washington, DC 20015 (US). OLSEN, Henrik, S. [DK/US]; 182 Kendrick Place #24, Gaithersburg, MD 29878 (US). BREWER, Laurie, A. [US/US]; Apartment 115, 410 Van Dyke Street, St. Paul, MN 55119-4321 (US). SHI, Yanggu [CN/US]; Apartment 102, 437 West Side Drive, Gaithersburg, MD 20878 (US). EBNER, Reinhard [DE/US]; 9906 Shelburne Terrace #316, Gaithersburg, MD 20878 (US). YOUNG, Paul [US/US]; 122 Beckwith Street, Gaithersburg, MD 20878 (US). GREENE, John, M. [US/US]; 872 Diamond Drive, Gaithersburg, MD 20878 (US). FLORENCE, Kimberly, A. [US/US]; 12805 Atlantic Avenue, Rockville, MD 20851 (US). FLORENCE, Charles [US/US]; 12805 Atlantic Avenue, Rockville, MD 20851 (US). DUAN, D., Roxanne [US/US]; 5515 Northfield Road, Bethesda, MD 20817 (US). JANAT, Fouad [US/US]; 140 High Street #202, Westerly, RI 02891 (US). ENDRESS, Gregory, A. [US/US]; 9729 Clagett Farm Drive, Potomac, MD 20854 (US). CARTER, Kenneth, C. [US/US]; 11601 Brandy Hall Lane, North Potomac, MD 20878 (US).

(74) Agents: BROOKES, A., Anders et al.; Human Genome Sciences, Inc., 9410 Key West Avenue, Rockville, MD 20850 (US).

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(54) Title: 148 HUMAN SECRETED PROTEINS

(57) Abstract

The present invention relates to novel human secreted proteins and isolated nucleic acids containing the coding regions of the genes encoding such proteins. Also provided are vectors, host cells, antibodies, and recombinant methods for producing human secreted proteins. The invention further relates to diagnostic and therapeutic methods useful for diagnosing and treating disorders related to these novel human secreted proteins.

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148 Human Secreted Proteins

Field of the Invention

This invention relates to newly identified polynucleotides and the polypeptides encoded by these polynucleotides, uses of such polynucleotides and polypeptides, and their production.

Background of the Invention

Unlike bacterium, which exist as a single compartment surrounded by a membrane, human cells and other eucaryotes are subdivided by membranes into many functionally distinct compartments. Each membrane-bounded compartment, or organelle, contains different proteins essential for the function of the organelle. The cell uses "sorting signals," which are amino acid motifs located within the protein, to target proteins to particular cellular organelles.

One type of sorting signal, called a signal sequence, a signal peptide, or a leader sequence, directs a class of proteins to an organelle called the endoplasmic reticulum (ER). The ER separates the membrane-bounded proteins from all other types of proteins. Once localized to the ER, both groups of proteins can be further directed to another organelle called the Golgi apparatus. Here, the Golgi distributes the proteins to vesicles, including secretory vesicles, the cell membrane, lysosomes, and the other organelles.

Proteins targeted to the ER by a signal sequence can be released into the extracellular space as a secreted protein. For example, vesicles containing secreted proteins can fuse with the cell membrane and release their contents into the extracellular space - a process called exocytosis. Exocytosis can occur constitutively or after receipt of a triggering signal. In the latter case, the proteins are stored in secretory vesicles (or secretory granules) until exocytosis is triggered. Similarly, proteins residing on the cell membrane can also be secreted into the extracellular space by proteolytic cleavage of a "linker" holding the protein to the membrane.

Despite the great progress made in recent years, only a small number of genes encoding human secreted proteins have been identified. These secreted proteins include the commercially valuable human insulin, interferon, Factor VIII, human growth hormone, tissue plasminogen activator, and erythropoeitin. Thus, in light of the pervasive role of secreted proteins in human physiology, a need exists for identifying and characterizing novel human secreted proteins and the genes that encode them. This knowledge will allow one to detect, to treat, and to prevent medical disorders by using secreted proteins or the genes that encode them.

Summary of the Invention

The present invention relates to novel polynucleotides and the encoded polypeptides. Moreover, the present invention relates to vectors, host cells, antibodies, and recombinant methods for producing the polypeptides and polynucleotides. Also provided are diagnostic methods for detecting disorders related to the polypeptides, and therapeutic methods for treating such disorders. The invention further relates to screening methods for identifying binding partners of the polypeptides.

Detailed Description

Definitions

The following definitions are provided to facilitate understanding of certain terms used throughout this specification.

In the present invention, "isolated" refers to material removed from its original environment (e.g., the natural environment if it is naturally occurring), and thus is altered "by the hand of man" from its natural state. For example, an isolated polynucleotide could be part of a vector or a composition of matter, or could be contained within a cell, and still be "isolated" because that vector, composition of matter, or particular cell is not the original environment of the polynucleotide.

In the present invention, a "secreted" protein refers to those proteins capable of being directed to the ER, secretory vesicles, or the extracellular space as a result of a signal sequence, as well as those proteins released into the extracellular space without necessarily containing a signal sequence. If the secreted protein is released into the extracellular space, the secreted protein can undergo extracellular processing to produce a "mature" protein. Release into the extracellular space can occur by many mechanisms, including exocytosis and proteolytic cleavage.

As used herein , a "polynucleotide" refers to a molecule having a nucleic acid sequence contained in SEQ ID NO:X or the cDNA contained within the clone deposited with the ATCC. For example, the polynucleotide can contain the nucleotide sequence of the full length cDNA sequence, including the 5' and 3' untranslated sequences, the coding region, with or without the signal sequence, the secreted protein coding region, as well as fragments, epitopes, domains, and variants of the nucleic acid sequence. Moreover, as used herein, a "polypeptide" refers to a molecule having the translated amino acid sequence generated from the polynucleotide as broadly defined.

In the present invention, the full length sequence identified as SEQ ID NO:X was often generated by overlapping sequences contained in multiple clones (contig

analysis). A representative clone containing all or most of the sequence for SEQ ID NO:X was deposited with the American Type Culture Collection ("ATCC"). As shown in Table 1, each clone is identified by a cDNA Clone ID (Identifier) and the ATCC Deposit Number. The ATCC is located at 10801 University Boulevard, Manassas, Virginia 20110-2209, USA. The ATCC deposit was made pursuant to the terms of the Budapest Treaty on the international recognition of the deposit of microorganisms for purposes of patent procedure.

A "polynucleotide" of the present invention also includes those polynucleotides capable of hybridizing, under stringent hybridization conditions, to sequences contained in SEQ ID NO:X, the complement thereof, or the cDNA within the clone deposited with the ATCC. "Stringent hybridization conditions" refers to an overnight incubation at 42° C in a solution comprising 50% formamide, 5x SSC (750 mM NaCl, 75 mM sodium citrate), 50 mM sodium phosphate (pH 7.6), 5x Denhardt's solution, 10% dextran sulfate, and 20 μg/ml denatured, sheared salmon sperm DNA, followed by washing the filters in 0.1x SSC at about 65°C.

Also contemplated are nucleic acid molecules that hybridize to the polynucleotides of the present invention at lower stringency hybridization conditions. Changes in the stringency of hybridization and signal detection are primarily accomplished through the manipulation of formamide concentration (lower percentages of formamide result in lowered stringency); salt conditions, or temperature. For example, lower stringency conditions include an overnight incubation at 37°C in a solution comprising 6X SSPE (20X SSPE = 3M NaCl; 0.2M NaH_2PO_4; 0.02M EDTA, pH 7.4), 0.5% SDS, 30% formamide, 100 ug/ml salmon sperm blocking DNA; followed by washes at 50°C with 1XSSPE, 0.1% SDS. In addition, to achieve even lower stringency, washes performed following stringent hybridization can be done at higher salt concentrations (e.g. 5X SSC).

Note that variations in the above conditions may be accomplished through the inclusion and/or substitution of alternate blocking reagents used to suppress background in hybridization experiments. Typical blocking reagents include Denhardt's reagent, BLOTTO, heparin, denatured salmon sperm DNA, and commercially available proprietary formulations. The inclusion of specific blocking reagents may require modification of the hybridization conditions described above, due to problems with compatibility.

Of course, a polynucleotide which hybridizes only to polyA+ sequences (such as any 3' terminal polyA+ tract of a cDNA shown in the sequence listing), or to a

complementary stretch of T (or U) residues, would not be included in the definition of "polynucleotide," since such a polynucleotide would hybridize to any nucleic acid molecule containing a poly (A) stretch or the complement thereof (e.g., practically any double-stranded cDNA clone).

The polynucleotide of the present invention can be composed of any polyribonucleotide or polydeoxribonucleotide, which may be unmodified RNA or DNA or modified RNA or DNA. For example, polynucleotides can be composed of single- and double-stranded DNA, DNA that is a mixture of single- and double-stranded regions, single- and double-stranded RNA, and RNA that is mixture of single- and double-stranded regions, hybrid molecules comprising DNA and RNA that may be single-stranded or, more typically, double-stranded or a mixture of single- and double-stranded regions. In addition, the polynucleotide can be composed of triple-stranded regions comprising RNA or DNA or both RNA and DNA. A polynucleotide may also contain one or more modified bases or DNA or RNA backbones modified for stability or for other reasons. "Modified" bases include, for example, tritylated bases and unusual bases such as inosine. A variety of modifications can be made to DNA and RNA; thus, "polynucleotide" embraces chemically, enzymatically, or metabolically modified forms.

The polypeptide of the present invention can be composed of amino acids joined to each other by peptide bonds or modified peptide bonds, i.e., peptide isosteres, and may contain amino acids other than the 20 gene-encoded amino acids. The polypeptides may be modified by either natural processes, such as posttranslational processing, or by chemical modification techniques which are well known in the art. Such modifications are well described in basic texts and in more detailed monographs, as well as in a voluminous research literature. Modifications can occur anywhere in a polypeptide, including the peptide backbone, the amino acid side-chains and the amino or carboxyl termini. It will be appreciated that the same type of modification may be present in the same or varying degrees at several sites in a given polypeptide. Also, a given polypeptide may contain many types of modifications. Polypeptides may be branched , for example, as a result of ubiquitination, and they may be cyclic, with or without branching. Cyclic, branched, and branched cyclic polypeptides may result from posttranslation natural processes or may be made by synthetic methods. Modifications include acetylation, acylation, ADP-ribosylation, amidation, covalent attachment of flavin, covalent attachment of a heme moiety, covalent attachment of a nucleotide or nucleotide derivative, covalent attachment of a lipid or lipid derivative, covalent attachment of phosphotidylinositol, cross-linking, cyclization, disulfide bond formation, demethylation, formation of covalent cross-links, formation of cysteine,

formation of pyroglutamate, formylation, gamma-carboxylation, glycosylation, GPI anchor formation, hydroxylation, iodination, methylation, myristoylation, oxidation, pegylation, proteolytic processing, phosphorylation, prenylation, racemization, selenoylation, sulfation, transfer-RNA mediated addition of amino acids to proteins such as arginylation, and ubiquitination. (See, for instance, PROTEINS - STRUCTURE AND MOLECULAR PROPERTIES, 2nd Ed., T. E. Creighton, W. H. Freeman and Company, New York (1993); POSTTRANSLATIONAL COVALENT MODIFICATION OF PROTEINS, B. C. Johnson, Ed., Academic Press, New York, pgs. 1-12 (1983); Seifter et al., Meth Enzymol 182:626-646 (1990); Rattan et al., Ann NY Acad Sci 663:48-62 (1992).)

"SEQ ID NO:X" refers to a polynucleotide sequence while "SEQ ID NO:Y" refers to a polypeptide sequence, both sequences identified by an integer specified in Table 1.

"A polypeptide having biological activity" refers to polypeptides exhibiting activity similar, but not necessarily identical to, an activity of a polypeptide of the present invention, including mature forms, as measured in a particular biological assay, with or without dose dependency. In the case where dose dependency does exist, it need not be identical to that of the polypeptide, but rather substantially similar to the dose-dependence in a given activity as compared to the polypeptide of the present invention (i.e., the candidate polypeptide will exhibit greater activity or not more than about 25-fold less and, preferably, not more than about tenfold less activity, and most preferably, not more than about three-fold less activity relative to the polypeptide of the present invention.)

Polynucleotides and Polypeptides of the Invention

FEATURES OF PROTEIN ENCODED BY GENE NO: 1

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:
MRFISQQSCECVRPCMDVYVCVYISIHVYMDAHVYLCRICKTNMR (SEQ ID NO:309), RILRWVNCMACDLYLNKAVSVCAHVWMCMCVYISLYMYTWMP MCIYVEYVKQT (SEQ ID NO:310), NPENQLEISFPPRRQKMKLTLDLQVSQS SLVHSLLSSDFFSVSKEGCLWKPILLPSHFL (SEQ ID NO:311), LQTQISN YLMFVLHILHRYTWASMYTCIEIYTHTYTSIHGRTHSQLC (SEQ ID NO:312),

IHMGIHVYMYRDIYTHIHIHTWAHTLTALLRYKSHAIQLTHLNIR (SEQ ID NO:313), and/or MKWIFTVLILTSCFFTAGICEDGICSRIQL RDKIVQSAFRQ (SEQ ID NO:314). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in neutrophils.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune disorders, particularly neutropenia and related conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.immune, hematopoeitic, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in neutrophils indicates that polynucleotides and polypeptides corresponding to this gene are useful for immune disorders. More specifically, this gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immunodeficiency diseases such as AIDS, leukemia, rheumatoid arthritis, granulomatous disease, inflammatory bowel disease, sepsis, acne, neutropenia, neutrophilia, psoriasis, hypersensitivities, such as T-cell mediated cytotoxicity; immune reactions to transplanted organs and tissues, such as host-versus-graft and graft-versus-host diseases, or autoimmunity disorders, such as autoimmune infertility, lense tissue injury, demyelination, systemic lupus erythematosis, drug induced hemolytic anemia, rheumatoid arthritis, Sjogren's disease, scleroderma and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:11 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 812 of SEQ ID NO:11, b is an integer of 15 to 826, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:11, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 2

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: KPCCPSVSNRSSVQMHQLPIQFLGQFEAHCIGFCRSFLETFYTHDPRAMHSFL SSISSPSLPFGFSRMTSQINHLHPSPLC (SEQ ID NO:315). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in neutrophils.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune disorders, particularly neutropenia. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:161 as residues: Asp-15 to Tyr-21, Pro-29 to Asn-39.

The tissue distribution in neutrophils indicates that polynucleotides and polypeptides corresponding to this gene are useful for immune disorders. Moreover,

the expression of this gene product indicates a role in the regulation of the proliferation; survival; differentiation; and/or activation of hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immunodeficiency diseases such as AIDS, leukemia, rheumatoid arthritis, granulomatous disease, inflammatory bowel disease, sepsis, acne, neutropenia, neutrophilia, psoriasis, hypersensitivities, such as T-cell mediated cytotoxicity; immune reactions to transplanted organs and tissues, such as host-versus-graft and graft-versus-host diseases, or autoimmunity disorders, such as autoimmune infertility, lense tissue injury, demyelination, systemic lupus erythematosis, drug induced hemolytic anemia, rheumatoid arthritis, Sjogren's disease, scleroderma and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:12 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 510 of SEQ ID NO:12, b is an integer of 15 to 524, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:12, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 3

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: SVFKINLKSFKQHEPWWPNRS (SEQ ID NO:316). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in neutrophils.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune disorders, including neutropenia. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:162 as residues: Met-1 to Arg-8, Leu-35 to Glu-41.

The tissue distribution in neutrophils indicates that polynucleotides and polypeptides corresponding to this gene are useful for immune disorders. More specifically, expression of this gene product indicates a role in the regulation of the proliferation; survival; differentiation; and/or activation of hematopoietic cell lineages, including blood stem cells. This gene product may also be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immunodeficiency diseases such as AIDS, leukemia, rheumatoid arthritis, granulomatous disease, inflammatory bowel disease, sepsis, acne, neutropenia, neutrophilia, psoriasis, hypersensitivities, such as T-cell mediated cytotoxicity; immune reactions to transplanted organs and tissues, such as host-versus-graft and graft-versus-host diseases, or autoimmunity disorders, such as autoimmune infertility, lense tissue injury, demyelination, systemic lupus erythematosis, drug induced hemolytic anemia, rheumatoid arthritis, Sjogren's disease, scleroderma and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:13 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 477 of SEQ ID NO:13, b is an integer of 15 to 491, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:13, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 4

This gene is expressed primarily in IL-1 and LPS induced neutrophils.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune disorders, including neutrophenia. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:163 as residues: Asn-45 to Thr-58.

The tissue distribution in neutrophils indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and/or prevention of a variety of immune disorders. In particular, this gene product may play a role in regulating the proliferation; survival; differentiation; and/or activation of hematopoietic cell lineages, including blood stem cells. Furthermore, this gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by

boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immunodeficiency diseases such as AIDS, leukemia, rheumatoid arthritis, granulomatous disease, inflammatory bowel disease, sepsis, acne, neutropenia, neutrophilia, psoriasis, hypersensitivities, such as T-cell mediated cytotoxicity; immune reactions to transplanted organs and tissues, such as host-versus-graft and graft-versus-host diseases, or autoimmunity disorders, such as autoimmune infertility, lense tissue injury, demyelination, systemic lupus erythematosis, drug induced hemolytic anemia, rheumatoid arthritis, Sjogren's disease, scleroderma and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:14 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 389 of SEQ ID NO:14, b is an integer of 15 to 403, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:14, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 5

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:
GTRSFSVPSYLRLTGSLMCYLLLLLIQTAELLIHPQGLQAVSNGESALKGTRPTF SSPFILVTEGRKEWEGVFLSSGWKGNTLSNYYISLVFYYSRILQPYFYCLWGK LEMVTLIRSVWRGINGGDKISVGFGKC (SEQ ID NO:317), WMERKHTVKLL YLLGFLLQNSPAIFLLSMGEVGDGDLD (SEQ ID NO:318) SNGESALKGTRP TFSSPFILVTE (SEQ ID NO:319), and/or LSNYYISLVFYYSRILQPYFYCLW (SEQ ID NO:320). Polynucleotides encoding these polypeptides are also encompassed by the invention.The gene encoding the disclosed cDNA is believed to reside on chromosome

17. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 17.

This gene is expressed primarily in the breast and brain.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune, reproductive, or neural disorders, such as cancers of the breast, lymph system and brain. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproductive, immune, and central nervous systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.immune, reproductive, neural, breast, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, breast milk, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:164 as residues: Leu-31 to Phe-38, Glu-47 to Trp-52.

The tissue distribution in breast and brain tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of cancers in the breast, lymph system, and brain. Moreover, the protein product of this gene may be useful for the detection/treatment of neurodegenerative disease states, behavioural disorders, or inflamatory conditions such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, meningitis, encephalitis, demyelinating diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses , autism, and altered bahaviors, including disorders in feeding, sleep patterns, balance, and preception. In addition, elevated expression of this gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or survival. Moreover, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular

system. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:15 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 799 of SEQ ID NO:15, b is an integer of 15 to 813, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:15, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 6

This gene is expressed primarily in neutrophils.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune disorders, such as neutropenia. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:165 as residues: Ser-49 to Leu-54.

The tissue distribution in neutrophils indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis, treatment, and/or prevention of a variety of immune disorders. Moreover, the expression of this gene product indicates a role in regulating the proliferation; survival; differentiation; and/or activation of hematopoietic cell lineages, including blood stem cells. This gene product

may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immunodeficiency diseases such as AIDS, leukemia, rheumatoid arthritis, granulomatous disease, inflammatory bowel disease, sepsis, acne, neutropenia, neutrophilia, psoriasis, hypersensitivities, such as T-cell mediated cytotoxicity; immune reactions to transplanted organs and tissues, such as host-versus-graft and graft-versus-host diseases, or autoimmunity disorders, such as autoimmune infertility, lense tissue injury, demyelination, systemic lupus erythematosis, drug induced hemolytic anemia, rheumatoid arthritis, Sjogren's disease, scleroderma and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:16 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 250 of SEQ ID NO:16, b is an integer of 15 to 264, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:16, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 7

The translation product of this gene shares sequence homology with neurotoxin which is thought to be important in neural diseases. In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: EKDFMQGSDAGHGGTHIYRALVQWPLAWVFYLSHAKTHWGEELRFSFRRKN LRLREAMRHETCQVTQLVA GKADSNLCLRDSETWFWPPLWAACSSLQATA CRLSSPSKGLGASRECPWLASGRAALVSFL (SEQ ID NO:321), SLRVKGRKPR LLYHSPARGTLWMLPGLCDCL ICRQWLVERSRLPRVGARTRFQSP SDTGWS

QLCQLPAV (SEQ ID NO:322), and/or ERSRLPRVGARTRFQSPSDTGWSQLC (SEQ ID NO:323). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in neutrophils.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune and neural diseases, particularly neurodegenerative disorders, such as Alzheimers or Parkinson's. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and neural systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.immune, hemaopoietic, neural, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:166 as residues: Gln-2 to Gly-10, Asp-77 to Phe-82.

The tissue distribution in neutrophils combined with the homology to the conserved neurotoxin protein indicates that polynucleotides and polypeptides corresponding to this gene are useful for immune and neural diseases. Similarly, the protein product of this gene may be useful for the detection/treatment of neurodegenerative disease states, behavioural disorders, or inflamatory conditions such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, meningitis, encephalitis, demyelinating diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses , autism, and altered bahaviors, including disorders in feeding, sleep patterns, balance, and preception. In addition, elevated expression of this gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or survival.Moreover, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular

system. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:17 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 506 of SEQ ID NO:17, b is an integer of 15 to 520, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:17, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 8

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: KHAFLMAHQFCVLSLAMQWSSCFQLVALPYLSL (SEQ ID NO:324). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in neutrophils.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune disorders, such as neutropenia. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in neutrophils indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis, treatment, and/or prevention of immune disorders. Furthermore, this gene product may be involved in the

regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immunodeficiency diseases such as AIDS, leukemia, rheumatoid arthritis, granulomatous disease, inflammatory bowel disease, sepsis, acne, neutropenia, neutrophilia, psoriasis, hypersensitivities, such as T-cell mediated cytotoxicity; immune reactions to transplanted organs and tissues, such as host-versus-graft and graft-versus-host diseases, or autoimmunity disorders, such as autoimmune infertility, lense tissue injury, demyelination, systemic lupus erythematosis, drug induced hemolytic anemia, rheumatoid arthritis, Sjogren's disease, scleroderma and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:18 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 979 of SEQ ID NO:18, b is an integer of 15 to 993, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:18, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 9

When tested against Jurket and PC12 cell lines, supernatants removed from cells containing this gene activated the GAS (gamma activating sequence) and EGR1 (early growth response gene 1) promoter elements. Thus, it is likely that this gene activates T-cells and sensory neurons through the JAK-STAT and EGR1 signal transduction pathways. GAS is a promoter element found upstream of many genes which are involved in the Jak-STAT pathway. The Jak-STAT pathway is a large, signal transduction pathway involved in the differentiation and proliferation of cells.

Therefore, activation of the Jak-STAT pathway, reflected by the binding of the GAS element, can be used to indicate proteins involved in the proliferation and differentiation of cells. EGR1 is a separate signal transduction pathway from Jak-STAT, genes containing the EGR1 promoter are induced in various tissues and cell types upon activation, leading the cells to undergo differentiation and proliferation. In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: MRPLCVLLPWPCWQWGGLGSASPIRPQAPPGQAAHAVP LPRAQHLAQRSRQ (SEQ ID NO:325). Polynucleotides encoding these polypeptides are also encompassed by the invention.The gene encoding the disclosed cDNA is believed to reside on chromosome 17. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 17.

This gene is expressed primarily in breast, lymph nodes, spleen, and to a lesser extent, in liver.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, reproductive, immune, or hepatic disorders, particularly cancers of the breast, liver, and lymph system. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the breast, liver and lymph system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.reproductive, breast, immune hematopoietic, hepatic, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, breast milk, bile. serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:168 as residues: Pro-54 to Gly-67.

The tissue distribution in breast and immune tissues combined with the detected EGR1 and GAS biological activity indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of cancers of the breast and lymph systems. Moreover, the GAS and EGR1 activity strongly indicates that the protein product of this gene may play an integral role in the regulation of cellular division, and may show utility in the diagnosis and treatment of cancer and other proliferative disorders. Similarly, such proliferative tissues rely on finely regulated

decisions involving cell differentiation and/or apoptosis. Thus this protein may also be involved in regulating apoptosis or tissue differentiation and, thus could be useful in cancer therapy. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:19 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 445 of SEQ ID NO:19, b is an integer of 15 to 459, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:19, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 10

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: ARGLRSPHGAAGVVRGDGGGKKGEDPYSPILFQ SERIPRLIYLPVISSEENS (SEQ ID NO:326). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in an LPS induced neutrophil cDNA library.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune system disorders, such as neutropenia. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in neutrophils indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of immune disorders, for example, in ameliorating an abberant neutrophil reponse to infectious agents. Similarly, the expression of this gene product may suggest a role in regulating the proliferation; survival; differentiation; and/or activation of hematopoietic cell lineages, including blood stem cells. This gene product may also be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immunodeficiency diseases such as AIDS, leukemia, rheumatoid arthritis, granulomatous disease, inflammatory bowel disease, sepsis, acne, neutropenia, neutrophilia, psoriasis, hypersensitivities, such as T-cell mediated cytotoxicity; immune reactions to transplanted organs and tissues, such as host-versus-graft and graft-versus-host diseases, or autoimmunity disorders, such as autoimmune infertility, lense tissue injury, demyelination, systemic lupus erythematosis, drug induced hemolytic anemia, rheumatoid arthritis, Sjogren's disease, scleroderma and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:20 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 541 of SEQ ID NO:20, b is an integer of 15 to 555, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:20, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 11

This gene is expressed primarily in prostate cancer.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, reproductive or immune system disorders, particularly prostate cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.reproductive, prostate, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, seminal fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:170 as residues: Pro-14 to Asp-25, Leu-51 to Val-63.

The tissue distribution in prostate tissues indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of reproductive system disorders such as cancer, particularly prostate cancer. Similarly, the expression within prostate cancer tissue, a cellular source marked by proliferating cells, indicates that this protein may play a role in the regulation of cellular division, and may show utility in the diagnosis and treatment of cancer and other proliferative disorders not limited to prostate tissue. Further, such tissues rely on decisions involving cell differentiation and/or apoptosis. Thus this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:21 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of

a-b, where a is any integer between 1 to 651 of SEQ ID NO:21, b is an integer of 15 to 665, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:21, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 12

The polynucleotide sequence of this gene may have a frame shift. Therefore the preferred signal peptide may reside in a frame other than the associated polynucleotides of this gene. In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: KSLSCSFLFLAFWLRRMGQTMCVCVCVCVCVRTWVYLYEPVKF RSPLIYV NLPTS (SEQ ID NO:327), and/or KLGFTMLARLVSNSXTSGDLPSSASQNAGI KGMSYRAWPYSYFLIRKNKQT NKQTKTNPQLGENKHCRNLKVSWSKNYFL (SEQ ID NO:328). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in T-cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune system disorders, particularly immunodeficiencies such as lupus and AIDS, or inflammatory disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in immune cells indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of a variety of immune system disorders. Moreover, this gene product may play a role in regulating the proliferation; survival; differentiation; and/or activation of hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may

also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immunodeficiency diseases such as AIDS, leukemia, rheumatoid arthritis, granulomatous disease, inflammatory bowel disease, sepsis, acne, neutropenia, neutrophilia, psoriasis, hypersensitivities, such as T-cell mediated cytotoxicity; immune reactions to transplanted organs and tissues, such as host-versus-graft and graft-versus-host diseases, or autoimmunity disorders, such as autoimmune infertility, lense tissue injury, demyelination, systemic lupus erythematosis, drug induced hemolytic anemia, rheumatoid arthritis, Sjogren's disease, scleroderma and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:22 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 763 of SEQ ID NO:22, b is an integer of 15 to 777, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:22, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 13

When tested against Jurket and U937 cell lines, supernatants removed from cells containing this gene activated the GAS (gamma activating sequence) promoter element. Thus, it is likely that this gene activates T-cells and promyelocytic cells through the JAK-STAT signal transduction pathway. GAS is a promoter element found upstream of many genes which are involved in the Jak-STAT pathway. The Jak-STAT pathway is a large, signal transduction pathway involved in the differentiation and proliferation of cells. Therefore, activation of the Jak-STAT pathway, reflected by the binding of the GAS element, can be used to indicate proteins involved in the

proliferation and differentiation of cells. In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: ERGQGGSSRNVAGSDLVFPAVFVSXLC (SEQ ID NO:329), GSPQGPSVALGSRQCWSRPLRRGGRGAAVEMWRGPTWCFRPSLCLCCVCGV SFGLYVPHGFSLSMCVSAP GSAWLSLVYSICLARGSMSXRXSSRXSLV ASGASVLLVCFWVXADPGVGVSVPRAXVSGLWWCVSPSACLXLAPTKPPP XLSFSLSIFPFSSNPSK (SEQ ID NO:330), and/or TIASLQPTALNHLIWRGW KRKGRLRERKRGXGGAWLGPXRGRQMDSHTTRDQRQXLGEQRHPLLGLXA PRSKPTKQMPQMQPGXPEKKXXLTWNHGLDRWNTQGTARQSLGQK HTWRD (SEQ ID NO:331). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in adipose tissue and the brain.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, metabolic or neural disorders, particularly obesity, and neurodegenerative or central nervous system disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the brain and central nervous system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.adipose, neural, immune, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in adipose and neural tissues, combined with the detected GAS biological activity indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of obesity and disorders of the brain and central nervous system. Similarly, the protein product of this gene may be useful for the detection/treatment of neurodegenerative disease states, behavioural disorders, or inflamatory conditions such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, meningitis, encephalitis, demyelinating diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses , autism, and altered bahaviors, including disorders in

feeding, sleep patterns, balance, and preception. In addition, elevated expression of this gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or survival. Moreover, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. In addition, the protein product of this gene may also be beneficial in detecting, treating, or preventing neural disorders which occur secondary to aberrant fatty acid metabolism in neural tissues, such as for aberrations in myelin sheath development, or associated autoimmune disorders of neural tissue or the overlying integument. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:23 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 526 of SEQ ID NO:23, b is an integer of 15 to 540, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:23, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 14

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: ARGPGTEGCEPWLQLQDRRER (SEQ ID NO:332), and/or MSSGTNSFFTLMALNSPTGDSGSRITVSPPRVHPVKSGRGRASDLLLTRFLAPR SALWS (SEQ ID NO:333). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in a cDNA library from IL-1 and LPS induced neutrophils.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are

not limited to, immune system disorders, such as neutropenia. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.immune, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in immune cells indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of conditions where lymphocytes show abberant response to an infectious agent. Similarly, this gene product may play a role in regulating the proliferation; survival; differentiation; and/or activation of hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immunodeficiency diseases such as AIDS, leukemia, rheumatoid arthritis, granulomatous disease, inflammatory bowel disease, sepsis, acne, neutropenia, neutrophilia, psoriasis, hypersensitivities, such as T-cell mediated cytotoxicity; immune reactions to transplanted organs and tissues, such as host-versus-graft and graft-versus-host diseases, or autoimmunity disorders, such as autoimmune infertility, lense tissue injury, demyelination, systemic lupus erythematosis, drug induced hemolytic anemia, rheumatoid arthritis, Sjogren's disease, scleroderma and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:24 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome.

Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 470 of SEQ ID NO:24, b is an integer of 15 to 484, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:24, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 15

This gene is expressed primarily in ovaries, tonsils, and CD34 positive bone marrow stem cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, reproductive, immune, developmental, or hematopoietic disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and reproductive systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.reproductive, ovarian, immune, tonsil, umbilical, developmental, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in ovarian and tonsil tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of immune and reproductive system disorders. Similarly, expression of this gene product in tonsils indicates a role in regulating the proliferation; survival; differentiation; and/or activation of hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immunodeficiency diseases such as AIDS, leukemia, rheumatoid arthritis, granulomatous disease, inflammatory bowel disease, sepsis, acne, neutropenia,

neutrophilia, psoriasis, hypersensitivities, such as T-cell mediated cytotoxicity; immune reactions to transplanted organs and tissues, such as host-versus-graft and graft-versus-host diseases, or autoimmunity disorders, such as autoimmune infertility, lense tissue injury, demyelination, systemic lupus erythematosis, drug induced hemolytic anemia, rheumatoid arthritis, Sjogren's disease, scleroderma and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:25 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 693 of SEQ ID NO:25, b is an integer of 15 to 707, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:25, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 16

When tested against U937 cell lines, supernatants removed from cells containing this gene activated the GAS (gamma activating sequence) promoter element. Thus, it is likely that this gene activates promyelocyctic cells through the JAK-STAT signal transduction pathway. GAS is a promoter element found upstream of many genes which are involved in the Jak-STAT pathway. The Jak-STAT pathway is a large, signal transduction pathway involved in the differentiation and proliferation of cells. Therefore, activation of the Jak-STAT pathway, reflected by the binding of the GAS element, can be used to indicate proteins involved in the proliferation and differentiation of cells. In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: HEYHLLSSRHILGSVLRLDVC SALWS (SEQ ID NO:334). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in IL-1 and LPS induced neutrophils.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a

biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune disorders, such as neutropenia. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in immune cells combined with the detected GAS biological activity indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis, treatment, and/or prevention of immune disorders. Specifically, the expression of this gene product in neutrophils indicates a role in regulating the proliferation; survival; differentiation; and/or activation of hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immunodeficiency diseases such as AIDS, leukemia, rheumatoid arthritis, granulomatous disease, inflammatory bowel disease, sepsis, acne, neutropenia, neutrophilia, psoriasis, hypersensitivities, such as T-cell mediated cytotoxicity; immune reactions to transplanted organs and tissues, such as host-versus-graft and graft-versus-host diseases, or autoimmunity disorders, such as autoimmune infertility, lense tissue injury, demyelination, systemic lupus erythematosis, drug induced hemolytic anemia, rheumatoid arthritis, Sjogren's disease, scleroderma and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:26 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the

scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 779 of SEQ ID NO:26, b is an integer of 15 to 793, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:26, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 17

This gene is expressed primarily in the spinal cord.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, any of a variety of nervous system and neuromuscular disorders, particularly amyotropic lateral sclerosis, musculuar dystrophy, and inherited and non-inherited forms of chorea. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous system and neuromuscular systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.neural, neuromuscular, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in spinal cord tissue indicates that this gene could be used for the treatment of spinal cord and related injuries. The protein product of this gene could be injected into the spinal cord to promote or control growth following injuring or degeneration. Alternatively cells expressing this gene could be injected or transferred into the spinal cord by other means as a treatment promoting the regulation of growth following spinal cord injury or degeneration. Moreover, polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states, behavioural disorders, or inflamatory conditions such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, meningitis, encephalitis, demyelinating diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries. ischemia and infarction,

aneurysms, hemorrhages, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses , autism, and altered bahaviors, including disorders in feeding, sleep patterns, balance, and preception. In addition, elevated expression of this gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or survival.Moreover, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:27 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 624 of SEQ ID NO:27, b is an integer of 15 to 638, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:27, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 18

When tested against U937 cell lines, supernatants removed from cells containing this gene activated the GAS (gamma activating sequence) promoter element. Thus, it is likely that this gene activates promyelocytic cells through the JAK-STAT signal transduction pathway. GAS is a promoter element found upstream of many genes which are involved in the Jak-STAT pathway. The Jak-STAT pathway is a large, signal transduction pathway involved in the differentiation and proliferation of cells. Therefore, activation of the Jak-STAT pathway, reflected by the binding of the GAS element, can be used to indicate proteins involved in the proliferation and differentiation of cells. In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:
FILFILEYDMLWKSLYTNSSAYGYVIASYFCLLGIKLLVKQKKXKKKTRGGAR

X PIRPXVESYYKSXAVVLQRRGLGKNLGG (SEQ ID NO:335). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in the adrenal gland.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, endocrine disorders, particularly disorders of the adrenal gland. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the adrenal gland, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.endocrine, adrenal, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in adrenal tissue, combined with the detected GAS biological activity indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection, treatment, and/or prevention of various endocrine disorders and cancers, particularly Addison's disease, Cushing's Syndrome, and disorders and/or cancers of the pancrease (e.g. diabetes mellitus), adrenal cortex, ovaries, pituitary (e.g., hyper-, hypopituitarism), thyroid (e.g. hyper-, hypothyroidism), parathyroid (e.g. hyper-,hypoparathyroidism) , hypothallamus, and testes. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:28 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 514 of SEQ ID NO:28, b is an integer of 15 to 528, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:28, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 19

This gene is expressed primarily in the placenta.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, reproductive system disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproductive system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.placental, reproductive, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:178 as residues: His-15 to Trp-20, Pro-48 to Ala-54.

The tissue distribution in placental tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of reproductive disorders. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:29 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 905 of SEQ ID NO:29, b is an integer of 15 to 919, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:29, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 20

The translation product of this gene shares sequence homology with human erythrocyte membrane anion-transport protein which is thought to be important in autoimmune diseases. Furthermore, the translation product of this gene also has homology to a human gnl|PID|d1026838 (AB012130) sodium bicarbonate cotransporter2 which is thought to be important in maintaining cellular homoestasis. Contact of cells with supernatant expressing the product of this gene was found to increase the permeability of the plasma membrane of enterocytes and renal mesangial cells to calcium. Thus it is likely that the product of this gene is involved in a signal transduction pathway that is initiated when the product binds a receptor on the surface of the enterocytes and renal mesangial cells. Thus, polynucleotides and polypeptides have uses which include, but are not limited to, activating cellular processes within enterocytes and renal mesangial cells. In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: RVSSHLFRLFGGLILDIKRKAPFFLSDFKDALSLQCLASILFLYCACMSPVITFG GLLGEATEG RIVSTKIGSGQAFSSSEASVCMHLSHYSYFYLKSLPTA (SEQ ID NO:336), FRLFGGLILDIKRKAPFFLSDFKD (SEQ ID NO:337), FLYCACMSPV ITFGGLLGEATEG (SEQ ID NO:338), and/or SSSEASVCMHLSHYSYFYLKSL (SEQ ID NO:339). Polynucleotides encoding these polypeptides are also encompassed by the invention. The gene encoding the disclosed cDNA is believed to reside on chromosome 3. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 3.

This gene is expressed primarily in human testes tumor.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune or reproductive disorders, particularly autoimmune diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.immune, reproductive, testicular, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, seminal fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression

level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in testis, the homology to an erythrocyte membrane antion-transport protein, in addition to, the detected calcium flux biological activity indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment of autoimmune diseases and other immune diseases such as cancer, particularly in, but not limited to, testicular tissue. Similarly, the translation product of this gene may be important in maintaining normal, cellular homeostasis. Therefore, the protein, as well as antibodies directed to the invention, is beneficial as a therapeutic in order to ameliorate conditions related to aberrant cellular pH regulation (for example, use antibodies to decrease the presence of the protein, or possibly in gene therapy applications in order to replace a defective form, or alternatively, increase the expression of either the endogenous or modified form of the invention). Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:30 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 850 of SEQ ID NO:30, b is an integer of 15 to 864, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:30, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 21

This gene is expressed primarily in the brain.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neural disorders, which include, but are not limited to, disorders of the brain and central nervous system, such as neurodegenerative conditions and/or depression. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s)

or cell type(s). For a number of disorders of the above tissues or cells, particularly of the brain and central nervous system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.neural, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:180 as residues: His-13 to Leu-18.

The tissue distribution in neural tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of disorders of the brain and central nervous system. Moreover, polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states, behavioural disorders, or inflamatory conditions such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, meningitis, encephalitis, demyelinating diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses , autism, and altered bahaviors, including disorders in feeding, sleep patterns, balance, and preception. In addition, elevated expression of this gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or survival.Moreover, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:31 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 905 of SEQ ID NO:31, b is an integer of 15 to

919, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:31, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 22

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: PCLQVIGIDFCRLLLMCLVLKRNLTVPFSSYSPLKTITCITSEQIAVVSNFFRQKL GVRAK FFQGACLHTSKVVICLNLPIISIQRADIRMWWLVVNTPYARGVNN (SEQ ID NO:340). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in the spinal cord.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, any of a variety of nervous system and neuromuscular disorders including, but not limited to, amyotropic lateral sclerosis, musculuar dystrophy, and inherited and non-inherited forms of chorea. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous system and neuromuscular systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.neural, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in spinal cord indicates that this gene could be used for the treatment of spinal cord injuries. The protein product of this gene could be injected into the spinal cord to promote or control growth following injuring or degeneration. Alternatively cells expressing this gene could be injected or transferred into the spinal cord by other means as a treatment promoting the growth or regulation of growth following spinal cord injury or degeneration. This gene may also be useful for the detection/treatment of neurodegenerative disease states, behavioural disorders, or inflamatory conditions such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, meningitis, encephalitis, demyelinating diseases,

peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses , autism, and altered bahaviors, including disorders in feeding, sleep patterns, balance, and preception. In addition, elevated expression of this gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or survival.Moreover, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:32 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 942 of SEQ ID NO:32, b is an integer of 15 to 956, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:32, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 23

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: VVSVCVLETGQLGPAALCRSV (SEQ ID NO:341). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in neutrophils.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune disorders, which include, nut are not limited to, inflammatory diseases or neutropenia. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification

of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.immune, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in neutrophils indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treament of the inflammatory conditions. Moreover, This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immunodeficiency diseases such as AIDS, leukemia, rheumatoid arthritis, granulomatous disease, inflammatory bowel disease, sepsis, acne, neutropenia, neutrophilia, psoriasis, hypersensitivities, such as T-cell mediated cytotoxicity; immune reactions to transplanted organs and tissues, such as host-versus-graft and graft-versus-host diseases, or autoimmunity disorders, such as autoimmune infertility, lense tissue injury, demyelination, systemic lupus erythematosis, drug induced hemolytic anemia, rheumatoid arthritis, Sjogren's disease, scleroderma and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:33 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 552 of SEQ ID NO:33, b is an integer of 15 to 566, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:33, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 24

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:
NISVHGFPVPCLRQRLQGPCHPKCCPHXISSGKPRSSFSPSSYHCKFSRNATLL VVPNIFSYMQSSFLIPQTSKYYILXPYAXTXRPIKXIFKQAKQ (SEQ ID NO:342), IYNDMMMEKKKTEVYQKRXSGDNTWGGKGLVAFVSSMEQGIHVQRCFIANL KFSSPGV (SEQ ID NO: 343), YDDGEKEDRGLPEEMXWGQHLGWQGPCSL CLKHGTGNPCTEMFYCQFKIFISWCLIPLVFARLGDFRDRPGWIFSWRYHLKH TVWGGYNIIML (SEQ ID NO: 344), TPGDENFKLAIKHLCTWIPCS (SEQ ID NO: 345), IRHEIFLTIESFCPSAPRGEDDDNLLRTSRVPDI (SEQ ID NO:346), IRGSIP GHKKMHLS FNVAAQWSLLKPLVLREEGALFLTHDQLESKNSWTLSIGPRV PYTYVVVTWSSALWDLPNQPLAGRKESGGSYGPISVTQSPHQAALKWFAKK KGKQSHSTVQLANILHVFXAPDXYHFVNTSLQLFLEYTVMCMLCENK QKT LGR (SEQ ID NO:347), EPEVTQVXSXELTFQ PRKAGAKVTAGKSHHQVIHWE FEIMLSSYSTDVPLWFLKFFSSNLPQTYFPHSGVKKWGSCFSLPWRDSPPLT FISLLSSHLTTFHLYHLHHGIICLGFSVYFHRAYTSLCILETAVGSY (SEQ ID NO:348), WSLLKPLVLREEGALFLTHDQLESK (SEQ ID NO:349), WFAKKK GKQSHSTVQLANILHV (SEQ ID NO:350), AGKSHHQVIHWEFEIMLSSYSTDVP (SEQ ID NO:351), and/or HGIICLGFSVYFHRAYTSLCILETAV (SEQ ID NO:352). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in smooth muscle.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, muscular or vascular disorders, which include, but are not limited to defective organ innervation; deficiencies in neuronal survival; peristaltic abnormalities; digestive disorders; perturbations of the vasculature. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the smooth muscle, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g., cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e.,

the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in smooth muscle tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and/or treatment of disorders that result from failures of normal smooth muscle function. For example, this gene product may represent a soluble factor produced by smooth muscle that regulates the innervation of organs or regulates the survival of neighboring neurons. Likewise, it may be involved in controlling the digestive process, and such actions as peristalsis. Similarly, it may be involved in controlling the vasculature in areas where smooth muscle surrounds the endothelium of blood vessels. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:34 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1550 of SEQ ID NO:34, b is an integer of 15 to 1564, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:34, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 25

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: KRLTINARVHLWTLKSVPL (SEQ ID NO:353), EYVFNMX XYSKSRAISPLSGPYTPRGTTPLPIIPEPGARQRDHPAS LKYAKIIQTKLFAL PYPKETSMKAVA (SEQ ID NO:354), and/or ETVPPRSSQFLKITXGPARSMSLIX XAIQNPEPYLLYLALIPQEALLLYLSSQSQVPGNETTPPV (SEQ ID NO:355). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in T-cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to. immune system disorders, which include, but are not limited to lupus,

inflammatory conditions, and immunodeficiencies such as AIDS. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:184 as residues: Ser-21 to Thr-34, Thr-38 to Glu-43.

The tissue distribution in immune cells indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of a variety of immune system disorders. Expression of this gene product in T-cells indicates a role in regulating the proliferation; survival; differentiation; and/or activation of hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immunodeficiency diseases such as AIDS, leukemia, rheumatoid arthritis, granulomatous disease, inflammatory bowel disease, sepsis, acne, neutropenia, neutrophilia, psoriasis, hypersensitivities, such as T-cell mediated cytotoxicity; immune reactions to transplanted organs and tissues, such as host-versus-graft and graft-versus-host diseases, or autoimmunity disorders, such as autoimmune infertility, lense tissue injury, demyelination, systemic lupus erythematosis, drug induced hemolytic anemia, rheumatoid arthritis, Sjogren's disease, scleroderma and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:35 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the

scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1021 of SEQ ID NO:35, b is an integer of 15 to 1035, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:35, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 26

The translation product of this gene was determined to have homology to the human IB3089A protein which is thought to play an important role in tumor suppression (See Genbank Accession No.gil3041877 (AF027734)).In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: NEVSFSLSLGFSPREFARWKVNNLAL ERKDFFSLPLPLAPEFIRNI RLLGRRPNLQQVTENLIKKYGTHFLLSATLGGKQHHNPKLIGCQTIGNNV KTRVA (SEQ ID NO:356), VPYFLIRFSVTCCRLGLLPRRRMFRIN SGARGNG KLKKSFLSRAK LFTFQRANSLGEKPRDKEKLTSFQSKRHKI (SEQ ID NO:357), and/or EMSAVLFNQIFCNLLQIGSPSKEANVPDKLWGKRQWQTEEVLPFQSQV VHLPTGKLPGGKAKG (SEQ ID NO:358). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in human fibrosarcoma.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, disorders afflicting endothelial, muscular, and extracellular matrix tissues, which include, but are not limited to fibrosarcomas and bladder cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the integumentary system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.endothelial, urogenital,renal, muscular, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:185 as residues: Pro-49 to Asp-68.

The tissue distribution in human fibrosarcoma indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of various cancers, particularly fibrosarcomas and fibroids. Moreover, the expression within cellular sources marked by proliferating cells indicates that this protein may play a role in the regulation of cellular division, and may show utility in the diagnosis and treatment of cancer and other proliferative disorders. Similarly, developmental tissues rely on decisions involving cell differentiation and/or apoptosis in pattern formation. Thus this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:36 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 606 of SEQ ID NO:36, b is an integer of 15 to 620, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:36, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 27

This gene is expressed primarily in human tonsil.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune or hematopoietic disorders, which include, but are not limited to inflammation and infectious diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types

(e.g.immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in tonsils indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis of inflammation and infectious diseases. Moreover, this gene product may play a role in regulating the proliferation; survival; differentiation; and/or activation of hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immunodeficiency diseases such as AIDS, leukemia, rheumatoid arthritis, granulomatous disease, inflammatory bowel disease, sepsis, acne, neutropenia, neutrophilia, psoriasis, hypersensitivities, such as T-cell mediated cytotoxicity; immune reactions to transplanted organs and tissues, such as host-versus-graft and graft-versus-host diseases, or autoimmunity disorders, such as autoimmune infertility, lense tissue injury, demyelination, systemic lupus erythematosis, drug induced hemolytic anemia, rheumatoid arthritis, Sjogren's disease, scleroderma and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:37 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 959 of SEQ ID NO:37, b is an integer of 15 to 973, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:37, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 28

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:
HYHGSGFLIKEFGSFLSLLCMLSCPYVFCHGMLEQEVPSSVVSPSTLDFPTSR TVNKFLFKLPSLWYSVIATQNGLKQKIRETFLFVQFSQMPRWHKLE (SEQ ID NO:359). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in adipose and brain.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to. metabolic or neural conditions, which include but are not limited to obesity and disorders of the brain and central nervous system. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.neural, metabolic tissues, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in neural and adipose tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of obesity and disorders of brain and central system. Moreover, polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states, behavioural disorders, or inflamatory conditions such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, meningitis, encephalitis, demyelinating diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses , autism, and altered bahaviors, including disorders in feeding, sleep patterns, balance, and preception. In addition. elevated expression of this gene product in regions of the brain

indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or survival. Moreover, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. In addition, considering the expression within both adipose tissue and brain indicates that the protein may be benefical either as a target for gene therapy, or as a novel therapeutic to ameliorate conditions affecting myelin sheath development in neurons, or other disorders involving neural tissue which occur secondary to aberrant fatty-acid metabolism. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:38 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 824 of SEQ ID NO:38, b is an integer of 15 to 838, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:38, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 29

The gene encoding the disclosed cDNA is thought to reside on chromosome 11. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 11. One embodiment of this gene comprises polypeptides of the following amino acid sequence: FCKHNGSKNVFSTFRTPAVLFTGIVALYIASGLTGFIGLEVVAQLFNC (SEQ ID NO:360). An additional embodiment is the polynucleotides encoding the polypeptides.

This gene is expressed primarily in suppressor T cells, endothelial cells, dendritic cells, and infant brain.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are

not limited to, immune system disorders related to abnormal activation of T cells. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. hematopoietic, developmental, neural, immune, endothelial, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:188 as residues: Tyr-14 to Leu-24, Pro-59 to Gln-66.

The tissue distribution in immune cells indicates that polynucleotides and polypeptides corresponding to this gene are useful for treating disorders of the immune system related to altered activation of T cells. Furthermore, this gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of immune disorders. Since the gene is expressed in cells of lymphoid origin, the gene or protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:39 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 593 of SEQ ID NO:39, b is an integer of 15 to

607, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:39, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 30

This gene is expressed primarily in the fetus and in tumor cell types.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, diseases of rapidly growing tissues such as cancers. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of rapdily growing tissues, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. fetal, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution of this gene primarily in the developing fetus indicates a role in the treatment and/or detection of developmental disorders and growth defects. In addition, expression in tumor cell types indicates a role in the detection and/or treatment of tumors. Furthermore, expression within fetal tissue and other cellular sources marked by proliferating cells indicates that this protein may play a role in the regulation of cellular division, and may show utility in the diagnosis and treatment of cancer and other proliferative disorders. Similarly, embryonic development also involves decisions involving cell differentiation and/or apoptosis in pattern formation. Thus this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:40 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more

polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 868 of SEQ ID NO:40, b is an integer of 15 to 882, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:40, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 31

This gene is expressed primarily in salivary gland, and to a lesser extent, in other tissues.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, digestive and immune disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the salivary gland and other glands of the exocrine system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. exocrine, digestive, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:190 as residues: Glu-25 to Gly-31, Tyr-62 to Thr-68.

The tissue distribution in salivary gland tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of digestive and immune system disorders. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:41 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of

a-b, where a is any integer between 1 to 945 of SEQ ID NO:41, b is an integer of 15 to 959, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:41, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 32

The gene encoding the disclosed cDNA is thought to reside on chromosome 12. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 12.

This gene is expressed primarily in brain tissue of adults, as well as infants.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neurodegenerative and behavioural disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central and peripheral nervous system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. brain, developmental, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:191 as residues: Ser-16 to Val-33.

The tissue distribution in neural tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states and behavioural disorders such as Alzheimers Disease, Parkinsons Disease, Huntintons Disease, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder and panic disorder. Furthermore, expression of this gene product within the brain indicates that it may be involved in neuronal survival; synapse formation; conductance; neural differentiation, etc. Such involvement may impact many processes, such as learning and cognition. Protein, as well as, antibodies directed against the protein may show utility as a tissue-specific marker and/or immunotherapy target for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:42 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 861 of SEQ ID NO:42, b is an integer of 15 to 875, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:42, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 33

This gene is expressed primarily in the synovium.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, diseases affecting the synovial lining including arthritis and autoimmune disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the musculo-skeletal system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. endothelial, skeletal, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for use as a factor that may protect against articular damage or promote growth of the cells in articulating joints. Furthermore, the expression of this gene product in synovium would suggest a role in the detection and treatment of disorders and conditions affecting the skeletal system, in particular osteoporosis as well as disorders afflicting connective tissues (e.g. arthritis, trauma, tendonitis, chrondomalacia and inflammation), such as in the diagnosis or treatment of various autoimmune disorders such as rheumatoid arthritis, lupus, scleroderma, and

dermatomyositis as well as dwarfism, spinal deformation, and specific joint abnormalities as well as chondrodysplasias (ie. spondyloepiphyseal dysplasia congenita, familial osteoarthritis, Atelosteogenesis type II, metaphyseal chondrodysplasia type Schmid). Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:43 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 616 of SEQ ID NO:43, b is an integer of 15 to 630, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:43, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 34

When tested against U937 Myeloid cell lines, supernatants removed from cells containing this gene activated the GAS assay. Thus, it is likely that this gene activates myeloid cells through the Jak-STAT signal transduction pathway. The gamma activating sequence (GAS) is a promoter element found upstream of many genes which are involved in the Jak-STAT pathway. The Jak-STAT pathway is a large, signal transduction pathway involved in the differentiation and proliferation of cells. Therefore, activation of the Jak-STAT pathway, reflected by the binding of the GAS element, can be used to indicate proteins involved in the proliferation and differentiation of cells.

This gene is expressed primarily in B-cell lymphoma cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune disorders, such as diseases of B-cell lineage including lymphomas lymphoblastic leukemias, myelomas and hairy cell leukemia. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a

number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:193 as residues: Lys-82 to Pro-90.

The tissue distribution and biological activity indicates that polynucleotides and polypeptides corresponding to this gene are useful for for the treatment and/or diagnosis of diseases of B-cell lineage including cancer. This factor may be useful in the terminal differentiation of malignant cells or may act as a growth factor for B-cell proliferation or differentiation, which is supported by the biological assay data. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:44 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 557 of SEQ ID NO:44, b is an integer of 15 to 571, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:44, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 35

When tested against U937 Myeloid cell lines, supernatants removed from cells containing this gene activated the GAS assay. Thus, it is likely that this gene activates myeloid cells through the Jak-STAT signal transduction pathway. The gamma activating sequence (GAS) is a promoter element found upstream of many genes which are involved in the Jak-STAT pathway. The Jak-STAT pathway is a large, signal transduction pathway involved in the differentiation and proliferation of cells. Therefore, activation of the Jak-STAT pathway, reflected by the binding of the GAS

element, can be used to indicate proteins involved in the proliferation and differentiation of cells.

This gene is expressed primarily in osteoclastoma derived stromal cells, placenta, pancreas and several tumor derived cells and to a lesser extent in brain, melanocytes, dendritic cells, and several other tissues.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, tumors of the pancreas, uterus, ovary, bone, or adrenal gland. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproductive system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. placenta, pancreas, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for treating or diagnosing tumors of the reproductive organs, pancreas, or bone marrow. Furthermore, polynucleotides and polypeptides corresponding to this gene are useful for the detection, treatment, and/or prevention of various endocrine disorders and cancers, particularly Addison's disease, Cushing's Syndrome, and disorders and/or cancers of the pancrease (e.g. diabetes mellitus), adrenal cortex, ovaries, pituitary (e.g., hyper-, hypopituitarism), thyroid (e.g. hyper-, hypothyroidism), parathyroid (e.g. hyper-,hypoparathyroidism) , hypothallamus, and testes. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:45 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 916 of SEQ ID NO:45, b is an integer of 15 to

930, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:45, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 36

When tested against K562 leukemia cell lines, supernatants removed from cells containing this gene activated the ISRE assay. Thus, it is likely that this gene activates leukemia cells through the Jak-STAT signal transduction pathway. The interferon-sensitive response element is a promoter element found upstream of many genes which are involved in the Jak-STAT pathway. The Jak-STAT pathway is a large, signal transduction pathway involved in the differentiation and proliferation of cells. Therefore, activation of the Jak-STAT pathway, reflected by the binding of the ISRE element, can be used to indicate proteins involved in the proliferation and differentiation of cells.

This gene is expressed primarily in kidney and to a lesser extent in brain.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, renal and nervous system disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the renal and nervous systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.renal, urogenital, endocrine, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:195 as residues: Lys-117 to Lys-126.

The tissue distribution of this gene in kidney tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and/or detection of renal disorders including kidney failure and Wilms Tumor in addition to the detection/treatment of neurodegenerative disease states and behavioural disorders such as Alzheimers Disease, Parkinsons Disease, Huntintons Disease,

schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder and panic disorder.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:46 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 423 of SEQ ID NO:46, b is an integer of 15 to 437, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:46, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 37

One embodiment of this gene comprises polypeptides of the following amino acid sequence:
MPKPGAATQRTLLCLPRLHPASGPPLPXAGPLRGLRQLPALPVPAASCRRRPAP RLCAAGPCTVGPAASPHAPPHGCPPPASLAHV AHRQSVSGTVCLGLRDGHV RGGCAAVRGXAALPWDAAAAGPDHMGVGSGPALL (SEQ ID NO:361). An additional embodiment is the polynucleotides encoding these polypeptides.

This gene is expressed primarily in pituitary and to a lesser extent in thymus and breast.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, metabolic and immune disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the endocrine and immune systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types or cell types (e.g. thymus, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution of this gene indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and/or detection of endocrine, metabolic, and immune disorders including growth and developmental defects, in addition to the treatment or detection of immune or hematopoietic disorders including arthritis, asthma, immunodeficiency diseases and leukemia. Protein, as well as, antibodies directed against the protein may show utility as a tissue-specific marker and/or immunotherapy target for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:47 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1010 of SEQ ID NO:47, b is an integer of 15 to 1024, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:47, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 38

This gene is expressed primarily in hemangiopericytoma.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, vascular disorders such as stroke, aneuyrism, cardiac arrest, hemorrhage. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the vascular system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. circulatory system, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:197 as residues: Cys-14 to Gly-23, Met-45 to Gly-51.

The tissue distribution of this gene solely in hemangiopericytoma indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and or detection of vascular disorders including hemorrhaging, aneuyrism, stroke and cardiac arrest. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:48 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 449 of SEQ ID NO:48, b is an integer of 15 to 463, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:48, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 39

The translation product of this gene shares sequence homology with a serine protease which is thought to be important in regulating the availibility and action of proteins in vivo.

This gene is expressed primarily in cerebellum.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to. disorders of the central nervous system related to abnormal growth factor regulation, including neurodegenerative conditions such as Alzheimers disease and psychiatric illness such as Schizophrenia. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the Central Nervous System, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. CNS, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression

level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:198 as residues: Ser-17 to Gln-22.

The tissue distribution in neural tissue, combined with the homology to serine proteases indicates that polynucleotides and polypeptides corresponding to this gene are useful for treating disorders of the central nervous system including neurodegenerative diseases and psychiatric disorders. Furthermore, expression of this gene product within cerebral tissue indicates that it may be involved in neuronal survival; synapse formation; conductance; neural differentiation, etc. Such involvement may impact many processes, such as learning and cognition. It may also be useful in the treatment of such neurodegenerative disorders as schizophrenia; ALS; or Alzheimer's.Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:49 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 871 of SEQ ID NO:49, b is an integer of 15 to 885, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:49, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 40

This gene is expressed primarily in CD34 depleted buffy coat.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, autoimmune disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.

immune, developmental, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in CD34 depleted buffy coat tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for treating disorders of the immune system including autoimmune diseases. Furthermore, expression of this gene product in CD34 depleted buffy coat indicates a role in the regulation of the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the gene or protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:50 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 833 of SEQ ID NO:50, b is an integer of 15 to 847, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:50, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 41

This gene is expressed primarily in B-cell lymphoma cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, diseases of B-cell lineage including lymphomas lymphoblastic leukemias, myelomas and hairy cell leukemia. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in immunce cells indicates that polynucleotides and polypeptides corresponding to this gene are useful for for the treatment and or diagnosis of diseases of B-cell lineage including cancer. This factor may be useful in the terminal differentiation of malignant cells or may act as a growth factor for B-cell proliferation or differentiation. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:51 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 566 of SEQ ID NO:51, b is an integer of 15 to 580, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:51, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 42

This gene is expressed primarily in brain and CD34 depleted buffy coat.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, autoimmune disorders particularly those of the central nervous system such as multiple sclerosis. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, neural, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:201 as residues: Pro-35 to Ala-40.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for treating autoimmune disorders such as multiple sclerosis. Furthermore, expression of this gene product in CD34 depleted buffy coat indicates a role in the regulation of the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the gene or protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:52 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 584 of SEQ ID NO:52, b is an integer of 15 to 598, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:52, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 43

This gene is expressed primarily in tissues of the brain.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neurological and neurodegenerative disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. CNS, brain, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in brain tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful as a neuronal protective agent and as a growth factor for cells of the central or peripheral nervous system. Furthermore, expression of this gene product within the brain indicates that it may be involved in neuronal survival; synapse formation; conductance; neural differentiation, etc. Such involvement may impact many processes, such as learning and cognition. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:53 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 557 of SEQ ID NO:53, b is an integer of 15 to 571, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:53, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 44

The gene encoding the disclosed cDNA is thought to reside on chromosome 9. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 9.

This gene is expressed primarily in embryo and fetal tissues.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, developmental disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the embryo and fetal tissues, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. fetal tissues, develpomental, cancerous and wounded tissues) or bodily fluids (e.g. lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in embryonic and fetal tissues indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of developmental disorders. Furthermore, the tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of cancer and other proliferative disorders. Expression within embryonic tissue and other cellular sources marked by proliferating cells indicates that

this protein may play a role in the regulation of cellular division. Similarly, embryonic development also involves decisions involving cell differentiation and/or apoptosis in pattern formation. Thus this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the abovelisted tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:54 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1233 of SEQ ID NO:54, b is an integer of 15 to 1247, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:54, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 45

The gene encoding the disclosed cDNA is thought to reside on chromosome 2. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 2.

This gene is expressed primarily in infant brain, placenta, some immune tissues, and, to a lesser extent, in other tissues.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, developmental and immune disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the early developmental stage tissues and immune tissues, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to

the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:204 as residues: Val-32 to Met-39, Leu-44 to Val-49.

The tissue distribution in fetal and immune tissues indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of developmental and immune disorders. Furthermore, the tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of cancer and other proliferative disorders. Expression within embryonic tissue and other cellular sources marked by proliferating cells indicates that this protein may play a role in the regulation of cellular division. Additionally, the expression in hematopoietic cells and tissues indicates that this protein may play a role in the proliferation, differentiation, and/or survival of hematopoietic cell lineages. In such an event, this gene may be useful in the treatment of lymphoproliferative disorders, and in the maintenance and differentiation of various hematopoietic lineages from early hematopoietic stem and committed progenitor cells. Similarly, embryonic development also involves decisions involving cell differentiation and/or apoptosis in pattern formation. Thus this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. The protein product of this gene is useful for the detection/treatment of neurodegenerative disease states, behavioural disorders, or inflamatory conditions such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, meningitis, encephalitis, demyelinating diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses . autism, and altered bahaviors, including disorders in feeding, sleep patterns, balance, and preception. In addition, elevated expression of this gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or survival.Moreover, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ

ID NO:55 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 834 of SEQ ID NO:55, b is an integer of 15 to 848, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:55, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 46

When tested against Jurkat T-cells, supernatants removed from cells containing this gene activated the GAS assay. Thus, it is likely that this gene activates T-cells through the Jak-STAT signal transduction pathway. The gamma activating sequence (GAS) is a promoter element found upstream of many genes which are involved in the Jak-STAT pathway. The Jak-STAT pathway is a large, signal transduction pathway involved in the differentiation and proliferation of cells. Therefore, activation of the Jak-STAT pathway, reflected by the binding of the GAS element, can be used to indicate proteins involved in the proliferation and differentiation of cells.

This gene is expressed primarily in brain tissues, and to a lesser extent, in T-cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neuronal disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the brain and immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, brain, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:205 as residues: Ser-33 to Ser-44.

The tissue distribution in T-cells indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of neuronal and immune system disorders. Furthermore, expression of this gene product in T-cells, as well as the observed biological activity of this gene product, indicates that this gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the gene or protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Alternatively, the expression within brain tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states, behavioural disorders. or inflamatory conditions such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, meningitis, encephalitis, demyelinating diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries. ischemia and infarction, aneurysms, hemorrhages, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses , autism, and altered bahaviors, including disorders in feeding, sleep patterns, balance, and preception. In addition, elevated expression of this gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or survival.Moreover, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:56 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more

polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 655 of SEQ ID NO:56, b is an integer of 15 to 669, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:56, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 47

When tested against U937 Myeloid cell lines, supernatants removed from cells containing this gene activated the GAS assay. Thus, it is likely that this gene activates myeloid cells through the Jak-STAT signal transduction pathway. The gamma activating sequence (GAS) is a promoter element found upstream of many genes which are involved in the Jak-STAT pathway. When tested against K562 leukemia cell lines, supernatants removed from cells containing this gene activated the ISRE assay. Thus, it is likely that this gene activates leukemia cells through the Jak-STAT signal transduction pathway. The interferon-sensitive response element is a promoter element found upstream of many genes which are involved in the Jak-STAT pathway. The Jak-STAT pathway is a large, signal transduction pathway involved in the differentiation and proliferation of cells. Therefore, activation of the Jak-STAT pathway, reflected by the binding of the GAS element, can be used to indicate proteins involved in the proliferation and differentiation of cells. Contact of cells with supernatant expressing the product of this gene increases the permeability of bovine chondrocytes to calcium. Thus, it is likely that the product of this gene is involved in a signal transduction pathway that is initiated when the product of this gene binds a receptor on the surface of the chondrocyte cells. Thus, polynucleotides and polypeptides have uses which include, but are not limited to, activating bone cells.

This gene is expressed primarily in breast and placenta.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, pregnancy disorders including miscarriage. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the breast and placenta , expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. placental tissues, breast, bone, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another

tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in both placenta and breast indicates a role for this protein in the treatment and/or detection of miscarriages in suspect individuals, of birth defects, of breast cancer, and female infertility. Furthermore, the biological assay data strongly indicates that the translation product of this gene is actively involved in the initiation of several signal transduction pathways and the activation of several cell types.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:57 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 666 of SEQ ID NO:57, b is an integer of 15 to 680, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:57, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 48

The gene encoding the disclosed cDNA is thought to reside on chromosome 11. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 11. One embodiment of this gene comprises the polypeptides of the following amino acid sequence:
MWGQPRPVDSVWSSSIPKKSVESNDNKSHLHKREH (SEQ ID NO:362),
MTTKAIFTKGNIDSLSFKSNMWSVYI (SEQ ID NO:363). An additional embodiment is the polynucleotides encoding these polypeptides.

This gene is expressed primarily in the pancreas.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, pancreatic related disorders such as diabetes. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the endocrine system, expression of this

gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. pancreas, endocrine, metabolic, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, bile, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution of this gene in pancreatic tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment/detection of endocrine disorders and metabolic disorders associated with the pancreas including diabetes, pancreatitis, and pancreatic cancer. Furthermore, the tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection, treatment, and/or prevention of various endocrine disorders and cancers, particularly Addison's disease, Cushing's Syndrome, and disorders and/or cancers of the pancrease (e.g. diabetes mellitus), adrenal cortex, ovaries, pituitary (e.g., hyper-, hypopituitarism), thyroid (e.g. hyper-, hypothyroidism), parathyroid (e.g. hyper-,hypoparathyroidism) , hypothallamus, and testes. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:58 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 510 of SEQ ID NO:58. b is an integer of 15 to 524, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:58, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 49

This gene is expressed primarily in chondrosarcoma tumors.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to. including diseases of the skeletal system, particularly with respect to the

cartilagenous structures and also cancer of these tissues. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the skeletal system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. bone, connective, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in chondrosarcoma tumors indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment/diagnosis of cartilage disorders including arthritis and cancer. Protein, as well as, antibodies directed against the protein may show utility as a tissue-specific marker and/or immunotherapy target for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:59 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 413 of SEQ ID NO:59, b is an integer of 15 to 427, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:59, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 50

The translation product of this gene shares sequence homology with sorbinwhich is thought to be important in the manufacture of vitamin C. Additionally, sorbin is thought to be important in the process of stimulating water and electrolyte absorption in various cells in the body. Porcine Sorbin has activity in stimulating water and electrolyte absorption across mucosa. It has been pursued as a regulator of electrolyte absorption in the nasal and enteric mucosa. This gene was identified in hypothalamus suggesting that it could play a role in the CNS regulation of water or electrolyte absorption.

This gene is expressed primarily in human hypothalamus tissue from a patient suffering from Alzheimer's disease.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neurologic disorders (eg. Alzheimer's disease). Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.neural, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:209 as residues: Leu-29 to Leu-37, Gln-65 to Asp-70, Gln-85 to Gly-95.

The tissue distribution in neural tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of Alzheimer's disease. Additionally, the translation product of this gene, based upon its homology to the porcine sorbin, could be useful for the detection and/or amelioration of disorders involving the CNS regulation of water or electrolyte absorption. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:60 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1249 of SEQ ID NO:60, b is an integer of 15 to 1263, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:60, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 51

This gene is expressed primarily in synovium, and to a lesser extent, in other tissues.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, synovial diseases such as synovial sarcoma. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the synovium, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. connective tissues, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in synovium indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of synovial diseases such as arthritis. Furthermore, the expression of this gene product in synovium would suggest a role in the detection and treatment of disorders and conditions affecting the skeletal system, in particular osteoporosis as well as disorders afflicting connective tissues (e.g. trauma, tendonitis, chrondomalacia and inflammation), such as in the diagnosis or treatment of various autoimmune disorders such as rheumatoid arthritis, lupus, scleroderma, and dermatomyositis as well as dwarfism, spinal deformation, and specific joint abnormalities as well as chondrodysplasias (ie. spondyloepiphyseal dysplasia congenita, familial osteoarthritis, Atelosteogenesis type II, metaphyseal chondrodysplasia type Schmid). Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:61 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of

a-b, where a is any integer between 1 to 706 of SEQ ID NO:61, b is an integer of 15 to 720, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:61, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 52

This gene is expressed primarily in immune tissues and fast-growing tissues, such as tumor and early-stage developmental tissues, and, to a lesser extent, in some other tissues.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune and growth related disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune tissues and fast-growing tissues, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. developmental, immune, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:211 as residues: Ala-28 to Ala-47.

The tissue distribution in immune tissues indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection and treatment of immune and growth related diorders. Furthermore, expression within embryonic tissue and other cellular sources marked by proliferating cells indicates that this protein may play a role in the regulation of cellular division, and may show utility in the diagnosis and treatment of cancer and other proliferative disorders. Similarly, embryonic development also involves decisions involving cell differentiation and/or apoptosis in pattern formation. Thus this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:62 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 575 of SEQ ID NO:62, b is an integer of 15 to 589, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:62, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 53

One embodiment of this gene comprises polypeptides of the following amino acid sequence: DSXLDRRPSGPDVKFLSNKHHFSMVC (SEQ ID NO:364). An additional embodiment is the polynucleotides encoding these polypeptides.

This gene is expressed primarily in spleen, and to a lesser extent, in a range of hematopoetic cell types.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune and hematopoeitic disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and hematopoetic systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. spleen, immune, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:212 as residues: Cys-25 to Trp-30.

The tissue distribution of this gene in spleen tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment or detection of immune or hematopoietic disorders including arthritis, asthma, immunodeficiency

diseases and leukemia. Expression of this gene product in spleen indicates a role in the regulation of the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the gene or protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:63 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 672 of SEQ ID NO:63, b is an integer of 15 to 686, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:63, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 54

This gene is expressed primarily in human normal breast, and to a lesser extent, in dendritic cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, glandular problems involving cells of epithelial origin including breast cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell

type(s). For a number of disorders of the above tissues or cells, particularly of the female endocrine system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. breast, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:213 as residues: Ser-32 to Asn-44.

The tissue distribution in breast tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis or treatment of both malignant and non-malignant problems of the breast tissues, including cancer. Alternatively. the expression in dendritic tissue indicates polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of hematopoetic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tissue-specific marker and/or immunotherapy target for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:64 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 438 of SEQ ID NO:64, b is an integer of 15 to 452, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:64, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 55

When tested against U937 Myeloid cell lines, supernatants removed from cells containing this gene activated the GAS assay. Thus, it is likely that this gene activates myeloid cells through the Jak-STAT signal transduction pathway. The gamma activating sequence (GAS) is a promoter element found upstream of many genes which are involved in the Jak-STAT pathway. The Jak-STAT pathway is a large, signal transduction pathway involved in the differentiation and proliferation of cells. Therefore, activation of the Jak-STAT pathway, reflected by the binding of the GAS element, can be used to indicate proteins involved in the proliferation and differentiation of cells.

This gene is expressed primarily in early stage human tissues, immune tissues, and to a lesser extent, in other tissues such as prostate.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, development and immune related diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and early stage human tissues, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, developmental, cancerous and wounded tissues) or bodily fluids (e.g. lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in embryonic and immune tissues indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of developmental and immune related diseases. The biological activity data supports the assertion that the translation product of this gene is useful in the treatment and/or diagnosis of diseases related to the immune system. Protein, as well as, antibodies directed against the protein may show utility as a tissue-specific marker and/or immunotherapy target for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:65 and may have been publicly available prior to conception of the present

invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 356 of SEQ ID NO:65, b is an integer of 15 to 370, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:65, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 56

The translation product of this gene shares sequence homology with medicago sativa salt-inducible protein.

This gene is expressed primarily in human chronic synovitis.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, skeletal or rheumatoid disorders, particularly, chronic synovitis. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the skeletal system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. connective tissues, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:215 as residues: Lys-30 to Ser-44, Pro-77 to His-82.

The tissue distribution in synovium indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis of and as a therapeutic agent for chronic synovitis. In addition, the expression of this gene product in synovium would suggest a role in the detection and treatment of disorders and conditions affecting the skeletal system, in particular osteoporosis as well as disorders afflicting connective tissues (e.g. arthritis, trauma, tendonitis, chrondomalacia and inflammation), such as in the diagnosis or treatment of various autoimmune disorders such as rheumatoid arthritis, lupus, scleroderma, and dermatomyositis as well as

dwarfism, spinal deformation, and specific joint abnormalities as well as chondrodysplasias (ie. spondyloepiphyseal dysplasia congenita, familial osteoarthritis, Atelosteogenesis type II, metaphyseal chondrodysplasia type Schmid). Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:66 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 973 of SEQ ID NO:66, b is an integer of 15 to 987, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:66, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 57

The translation product of this gene shares high sequence homology with the rat and mouse peroxisomal membrane proteins [gil297437], which appears to play a crucial role in transporting proteins into the organelle. Some human genetic disorders involving peroxisome biogenesis, such as Zellweger syndrome, may be caused by genetic defects of the import machinery located in the peroxisomal membrane. When tested against fibroblast cell lines, supernatants removed from cells containing this gene activated the EGR1 assay. Thus, it is likely that this gene activates fibroblast cells through a signal transduction pathway. Early growth response 1 (EGR1) is a promoter associated with certain genes that induces various tissues and cell types upon activation, leading the cells to undergo differentiation and proliferation.

This gene is expressed primarily in normal human liver.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, diseases of the hepatic system. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the hepatic disorders and liver metabolic

diseases, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. liver, cancerous and wounded tissues) or bodily fluids (e.g. lymph, bile, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:216 as residues: Lys-57 to Ser-66.

The tissue distribution in liver indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of diseases relating to the liver. Furthermore, the homology indicates that the translational product of this gene may be useful in the detection and treatment of a number of disorders resulting from the improper transport of proteins into the organelle due to defects in peroxisomal membrane proteins, such as Zellweger syndrome. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:67 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1004 of SEQ ID NO:67, b is an integer of 15 to 1018, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:67, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 58

The gene encoding the disclosed cDNA is thought to reside on chromosome 4. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 4.

This gene is expressed primarily in human fetal dura mater.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are

not limited to, developmental or neurologic disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. brain, developmental, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:217 as residues: Ala-19 to Lys-34.

The tissue distribution in neural tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of neurological diseases. Furthermore, the tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states and behavioural disorders such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses , autism, and altered bahaviors, including disorders in feeding, sleep patterns, balance, and preception. In addition, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, and/or sexually-linked disorders. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:68 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 748 of SEQ ID NO:68, b is an integer of 15 to 762, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:68, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 59

The gene encoding the disclosed cDNA is thought to reside on chromosome 16. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 16.

This gene is expressed primarily in T helper cell and human uterine cancer.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, relating to hemopoietic and uterus disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and female reproductive system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, reproductive, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in T-helper cells and uterine tissues indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of disorders relating to both the immune and female reproductive systems. Expression of this gene product in T-cells indicates a role in the regulation of the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the gene or protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell

types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:69 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 616 of SEQ ID NO:69, b is an integer of 15 to 630, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:69, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 60

This gene is expressed primarily in human fetal epithelium, and to a lesser extent, in testes.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, developmental or reproductive disorders, in addition to diseases of the integumentary system. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the diseases relating to the epithelium, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. epithelium, testes, developmental, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, amniotic fluid, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in fetal epithelium and testes indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of epithelium related diseases. In addition, polynucleotides and polypeptides corresponding to this gene are useful for the treatment, diagnosis, and/or prevention of various skin disorders including congenital disorders (i.e. nevi, moles,

freckles, Mongolian spots, hemangiomas, port-wine syndrome), integumentary tumors (i.e. keratoses, Bowen's disease, basal cell carcinoma, squamous cell carcinoma, malignant melanoma, Paget's disease, mycosis fungoides, and Kaposi's sarcoma), injuries and inflammation of the skin (i.e.wounds, rashes, prickly heat disorder, psoriasis, dermatitis), atherosclerosis, uticaria, eczema, photosensitivity, autoimmune disorders (i.e. lupus erythematosus, vitiligo, dermatomyositis, morphea, scleroderma, pemphigoid, and pemphigus), keloids, striae, erythema, petechiae, purpura, and xanthelasma. Moreover, such disorders may predispose increased susceptibility to viral and bacterial infections of the skin (i.e. cold sores, warts, chickenpox, molluscum contagiosum, herpes zoster, boils, cellulitis, erysipelas, impetigo, tinea, althletes foot, and ringworm). Furthermore, the tissue distribution also indicates that the protein product of this gene is useful for the treatment and diagnosis of conditions concerning proper testicular function (e.g. endocrine function, sperm maturation), as well as cancer. Therefore, this gene product is useful in the treatment of male infertility and/or impotence. This gene product is also useful in assays designed to identify binding agents as such agents (antagonists) are useful as male contraceptive agents. Similarly, the protein is believed to by useful in the treatment and/or diagnosis of testicular cancer. The testes are also a site of active gene expression of transcripts that may be expressed, particularly at low levels, in other tissues of the body. Therefore, this gene product may be expressed in other specific tissues or organs where it may play related functional roles in other processes, such as hematopoiesis, inflammation, bone formation, and kidney function, to name a few possible target indications.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:70 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 926 of SEQ ID NO:70, b is an integer of 15 to 940, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:70, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 61

When tested against both U937 Myeloid cell and Jurkat T-cell cell lines, supernatants removed from cells containing this gene activated the GAS assay. Thus, it is likely that this gene activates both T-cells and myeloid cells through the Jak-STAT signal transduction pathway. The gamma activating sequence (GAS) is a promoter element found upstream of many genes which are involved in the Jak-STAT pathway. The Jak-STAT pathway is a large, signal transduction pathway involved in the differentiation and proliferation of cells. Therefore, activation of the Jak-STAT pathway, reflected by the binding of the GAS element, can be used to indicate proteins involved in the proliferation and differentiation of cells.

This gene is expressed primarily in human adult lymph node and in early stage human lung.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune disorders, lymphatitis and pulmonary disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system and respiratory system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in adult lymph indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of diseases relating to the immune system and respiratory system. Furthermore, expression of this gene product in lymph nodes indicates a role in the regulation of the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the gene or protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency

diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. The biological activity data supports the notion that the translation product of this gene is an activator of various cells of the immune system, and thus could play an important role in the activities of the immune system.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:71 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1089 of SEQ ID NO:71, b is an integer of 15 to 1103, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:71, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 62

This gene is expressed primarily in glioblastoma and anergic T-cell.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neural and immune disorders, such as glioblastosis cerebri. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the CNS and immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, neural, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in T-cells indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of disorders relating to the CNS and the immune system. Furthermore, expression of this gene product in T-cells indicates a role in the regulation of the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the gene or protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:72 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 885 of SEQ ID NO:72, b is an integer of 15 to 899, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:72, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 63

One embodiment of this gene comprises polypeptides of the following amino acid sequence:

CLAEAVSVIQSIPIFNETGRFSFTLPYPVKIKVRFSFFLQIYLIMIFLGLYINFRHLY KQRRRRYGQKKKRSTKKKDLDGFLPV (SEQ ID NO:365). An additional embodiment is the polynucleotides encoding these polypeptides.

This gene is expressed primarily in keratinocytes and brain.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, integumentary, or neurological and behavioural disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the nervous systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. brain, integumentary, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution of this gene in neural tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and/or detection of neurodegenerative disease states and behavioural disorders such as Alzheimer's Disease, Parkinson's Disease, Huntinton's Disease, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder and panic disorder. Alternatively, expression within keratinocytes indicates polynucleotides and polypeptides corresponding to this gene are useful for the treatment, diagnosis, and/or prevention of various skin disorders including congenital disorders (i.e. nevi, moles, freckles, Mongolian spots, hemangiomas, port-wine syndrome), integumentary tumors (i.e. keratoses, Bowen's disease, basal cell carcinoma, squamous cell carcinoma, malignant melanoma, Paget's disease, mycosis fungoides, and Kaposi's sarcoma), injuries and inflammation of the skin (i.e.wounds, rashes, prickly heat disorder, psoriasis, dermatitis), atherosclerosis, uticaria, eczema, photosensitivity, autoimmune disorders (i.e. lupus erythematosus, vitiligo, dermatomyositis, morphea, scleroderma, pemphigoid, and pemphigus), keloids, striae, erythema, petechiae, purpura, and xanthelasma. In addition, such disorders may predispose increased susceptibility to viral and bacterial infections of the skin (i.e. cold sores, warts, chickenpox, molluscum contagiosum, herpes zoster, boils, cellulitis, erysipelas, impetigo, tinea, althletes foot, and ringworm). Moreover, the protein product of this gene may also be useful for the treatment or diagnosis of various connective tissue disorders such as arthritis, trauma, tendonitis, chrondomalacia and inflammation, autoimmune disorders such as rheumatoid arthritis, lupus, scleroderma, and dermatomyositis as well as dwarfism, spinal deformation, and specific joint abnormalities as well as chondrodysplasias (ie. spondyloepiphyseal dysplasia

congenita, familial osteoarthritis, Atelosteogenesis type II, metaphyseal chondrodysplasia type Schmid). Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:73 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 535 of SEQ ID NO:73, b is an integer of 15 to 549, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:73, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 64

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: LCSTPVPTLFCPRIVLEVLVVLRSISEQCRRVSSQVTVASELRHRQWVERTLRSR QRQNYLR (SEQ ID NO:366). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in osteoclastoma.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, skeletal disorders, and diseases of the haemopoietic and immune system, particularly cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the bones, immune and haemopoietic system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.skeletal,hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard

gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:223 as residues: Ser-59 to Glu-67.

The tissue distribution in osteoclastoma tissues indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatement and diagnosis of disorders of the bones, immune and haemopoietic systems and cancer. Moreover, the protein may play a role as a therapeutic in the detection and treatment of disorders and conditions affecting the skeletal system, in particular osteoporosis, bone cancer, as well as, disorders afflicting connective tissues (e.g. arthritis, trauma, tendonitis, chrondomalacia and inflammation), such as in the diagnosis or treatment of various autoimmune disorders. For example, in rheumatoid arthritis, lupus, scleroderma, and dermatomyositis as well as dwarfism, spinal deformation, and specific joint abnormalities as well as chondrodysplasias (ie. spondyloepiphyseal dysplasia congenita, familial osteoarthritis, Atelosteogenesis type II, metaphyseal chondrodysplasia type Schmid). Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:74 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 576 of SEQ ID NO:74, b is an integer of 15 to 590, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:74, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 65

When tested against dermal fibroblast cell lines, supernatants removed from cells containing this gene activated the EGR1 (early growth response gene 1) promoter element. Thus, it is likely that this gene activates fibroblast cells through the EGR1 signal transduction pathway. EGR1 is a separate signal transduction pathway from Jak-STAT, genes containing the EGR1 promoter are induced in various tissues and cell

types upon activation, leading the cells to undergo differentiation and proliferation. In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:

ARGETAYDGAAVEFQEPLSSCLFSSLNPHHWPTLGVGRPVMLTLEDKD (SEQ ID NO:367), ELLQCQMLEASTLIHLHHPRPGFPALCSFLGFRHHLHHDALCIRV LPEDLEAKLCVSLHQLLHRGLCLPGFGAACPGDQGSEDEARPPAVLRAVALLR AGLRHLSVHSGWYHLPH SRNGLPLLALVVHFPEYGGGPREPVPGQSG EFGRRTELSTKGDTGDSRNSHLAQDMASLPFFKPCECTHV AVCSPPHPLCQ YLCL (SEQ ID NO:368), LQCQMLEASTLIHLHHPRPGFPALCSFL (SEQ ID NO:369), HQLLHRGLCLPGFGAACPGDQGSEDEARPPA (SEQ ID NO:370), and/or LALVVHFPEYGGGPREPVPGQSGEFGR (SEQ ID NO:371) . Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in testes.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, male reproductive and endocrine disorders, cancer, particularly testicular cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the male reproductive and endocrine systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.reproductive, testes, endcrine, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, seminal fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:224 as residues: Lys-53 to Leu-60, Pro-94 to Gln-99, Ser-176 to Gly-184, Ser-199 to Val-207.

The tissue distribution in testes, combined with the detected EGR1 biological activity indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of male reproductive and endocrine disorders, including aberrant testicular function (e.g. endocrine function, sperm maturation). Moreover, in light of the EGR1 activity, it may also be useful in the diagnosis and treatment of a variety of proliferative disorders, especially testicular cancer. Protein, as

well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:75 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1042 of SEQ ID NO:75, b is an integer of 15 to 1056, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:75, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 66

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: QSWTAPAARLPMALPQMCDGSHLASTLRYC (SEQ ID NO:372), QSAAQWFWWPGRSASLGGAKGMQPPSLASWPXPRSIRCL RAPAPC SXPSASSAAVQVACCCSLACCGPSRPASQGHLRWDPYHLSRDLYYLTVESSEK ESCRTPKVVDI PTYEEAVSFPVAEGPPTPPAYPTEEALEPSGSRDALLSTQPA WPPPSYESISLALDAVSAETTPSATRSC SGLVQTARGGS (SEQ ID NO:373), GSTGLWRGDRGPIEGGPGMLAL TDHSRVSFPVAEGPPTPPAYPTEEAL EPSGSRDALLSSVXGASWPGWAVASPSLHQAKQSVPATRTTVPLTVM Q (SEQ ID NO:374), QWFWWPGRSASLGGAKGMQPPSLASWP (SEQ ID NO:375), SSAA VQVACCCSLACCGPSRPASQGHLRW (SEQ ID NO:376), VSFPVAEGPPTPPAYP TEEALEPSGSRDALLS (SEQ ID NO:377), and/or RVSFPVAEGPPTPPAYPTEE ALEPSG (SEQ ID NO:378). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in pituitary gland.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, endocrine disorders, such as dwarfism. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the endocrine system, expression of this

gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.endocrine, immune, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in pituitary indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of disorders of the pituitary gland and endocrine system. Moreover, considering the vital importance of the pituitary in serving as a master regulator for various endocrine glands, the protein product of this gene would also be useful for the detection, treatment, and/or prevention of various endocrine disorders and cancers, particularly Addison's disease, Cushing's Syndrome, and disorders and/or cancers of the pancrease (e.g. diabetes mellitus), adrenal cortex, ovaries, pituitary (e.g., hyper-, hypopituitarism), thyroid (e.g. hyper-, hypothyroidism), parathyroid (e.g. hyper-,hypoparathyroidism) , hypothallamus, and testes. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:76 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 916 of SEQ ID NO:76, b is an integer of 15 to 930, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:76, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 67

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:
SNEILLSFPQNYYIQWLNGSLIHGLWNLASLFSNLCLFVLMPFAFFFLESEGFA GLKKGIRARILETLVM LLLLALLILGIVWVASALIDNDAAS (SEQ ID NO:379). Polynucleotides encoding these polypeptides are also encompassed by the

invention.The gene encoding the disclosed cDNA is believed to reside on chromosome 7. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 7.

This gene is expressed primarily in the developing brain, liver and heart,and to a lesser extent, in cancerous tissues.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, developmental,neural, hepatic, or cardiopulmonary and haemopietic disorders, in addition to cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the fetal tissues and the haemopoietic and neural systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.developmental, neural, hematopoietic, hepatic, cardiovascular, pulmonary, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, amniotic fluid, bile, serum, pulmponary surfactant or sputum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:226 as residues: Glu-67 to Asn-74, Glu-88 to Asn-93, Lys-95 to Ser-105, Arg-152 to Ala-164, Ala-204 to Arg-210, Phe-254 to Thr-262, Pro-295 to His-311.

The tissue distribution in developing brain indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatment and diagnosis of haemopoietic and developmental diseases and cancers. Moreover, polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states, behavioural disorders, or inflamatory conditions such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, meningitis, encephalitis, demyelinating diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses , autism, and altered bahaviors, including disorders in feeding, sleep patterns, balance, and preception. In addition, elevated expression of this gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or

neuronal differentiation or survival.Moreover, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Alternatively, the relatively specific expression of this gene product during embryogenesis indicates that it may be a key player in the proliferation, maintenance, and/or differentiation of various cell types during development. It may also act as a morphogen to control cell and tissue type specification. Because of potential roles in proliferation and differentiation, this gene product may have applications in the adult for tissue regeneration and the treatment of cancers, which include, but are not limited to the following tissues or cells: pulmonary, immune, neural, hematopoietic, or hepatic tissues. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:77 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 4449 of SEQ ID NO:77, b is an integer of 15 to 4463, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:77, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 68

The translation product of this gene shares sequence homology with a putative yeast transmembrane protein which may play an important role in intercellular signalling, intracellular transport, or regulation of cellular homeostasis. In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: PTRPVLLLAINGVTECFTFAAMSKEEVDRYNFV (SEQ ID NO:380), and/or NDKKLLFLKGFWSSLKNETPPPHFRLRMVTGVSCSGTLWCLISGV AVTPLQSPQWG SYTECVPPTELPIAGPGASGVQASLKSRHFVSASGHT (SEQ ID NO:381). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in pulmonary, immune cells, epididymus, and testis tissues.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, disorders of the reproductive organs, immune, and pulmonary systems, in addition to endothelial and epithelial tissues. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune, respiratory and reproductive systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.pulmonary, immune, reproductive, testes, epididymus, endothelial, epithelial, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, seminal fluid, pulmonary surfactant or sputum, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:227 as residues: Arg-45 to Thr-52, Tyr-60 to Gly-66, Ala-87 to Trp-92, Leu-105 to Ser-115.

The tissue distribution and homology to putative transmembrane protein indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatment and diagnosis of diseases of the reproductive, pulmonary and immune system. Moreover, the protein product of this gene may be useful in the diagnosis, treatment, and/or prevention of a variety of male reproductive disorders, which include, but are not limited to, aberrant testicular function, male sterility, impotence, or related endocrine disorders. Protein may also serve a role as a contraceptive. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:78 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 777 of SEQ ID NO:78, b is an integer of 15 to

791, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:78, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 69

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: SENRIYRNGLEKMRREVTIGRSSSICLDQQVKAGNAVHHQWLKYVCWMVVVV GGSGVGDGG NLGM (SEQ ID NO:382). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in PMA induced T cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune or hematopoietic disorders, such as inflammatory or immunodeficiency conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:228 as residues: Ser-62 to Thr-73, Phe-80 to Gln-88.

The tissue distribution in T-cells indicates that polynucleotides and polypeptides corresponding to this gene are useful for study and diagnosis of immune system disorders. More specifically, this gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immunodeficiency diseases such as AIDS, leukemia, rheumatoid arthritis, granulomatous disease, inflammatory bowel disease,

sepsis, acne, neutropenia, neutrophilia, psoriasis, hypersensitivities, such as T-cell mediated cytotoxicity; immune reactions to transplanted organs and tissues, such as host-versus-graft and graft-versus-host diseases, or autoimmunity disorders, such as autoimmune infertility, lense tissue injury, demyelination, systemic lupus erythematosis, drug induced hemolytic anemia, rheumatoid arthritis, Sjogren's disease, scleroderma and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:79 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1278 of SEQ ID NO:79, b is an integer of 15 to 1292, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:79, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 70

This gene is expressed primarily in monocytes.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune or hematopoietic disorders, which include, but are not limited to, leukemias, lymphomas, AIDS, arthritis and asthma. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard

gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in monocytes indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of immune disorders including: leukemias, lymphomas, immunodeficiencies (e.g. AIDS), immuno-supressive conditions (transplantation) and hematopoietic disorders. In addition this gene product may be applicable in conditions of general microbial infection, inflammation or cancer. Moreover, this gene may also be useful for the treatment and diagnosis of hematopoetic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:80 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1269 of SEQ ID NO:80, b is an integer of 15 to 1283, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:80, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 71

When tested against dermal fibroblast cell lines, supernatants removed from cells containing this gene activated the EGR1 (early growth response gene 1) promoter element. Thus, it is likely that this gene activates fibroblast cells through the EGR1 signal transduction pathway. EGR1 is a separate signal transduction pathway from Jak-

STAT, genes containing the EGR1 promoter are induced in various tissues and cell types upon activation, leading the cells to undergo differentiation and proliferation. In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:

NWSGRRLRMWPSAALSPAVSSPALALTSPPKPLKGEVWLRWKLLGSRAVGLF AF IALGTQSPLLHRACLPVRQSWGCSEHKAYPILRLQPDLETQVGPGHGVN WDLRTQIRTIGELGGDGGCSE MRPLF (SEQ ID NO:383), and/or NLFSTPCKRQ KLIKLEWTEAPNVALRCSLSCSLIPGLSPDLSSEAPEGRSVAKMEIARQQSCWL VCI YCFRNPESTLAPGLPACEAELGLLRAQGLPHPASPARLGNTGGAWPR SKLGSQNTN (SEQ ID NO:384), SSPALALTSPPKPLKGEVWLRWKLLG (SEQ ID NO:385), EHKAYPILRLQPDLETQVGPGHGVNWDL (SEQ ID NO:386), and/or ALRCSLSCSLIPGLSPDLSSEAPEGRSV (SEQ ID NO:387). Polynucleotides encoding these polypeptides are also encompassed by the invention.The gene encoding the disclosed cDNA is believed to reside on chromosome 11. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 11.

This gene is expressed primarily in placenta.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, developmental anomalies, fetal deficiencies, pre-natal disorders and cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproductive system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.reproductive, placental, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:230 as residues: Gly-22 to Gly-29, Gln-37 to Ala-44.

The tissue distribution in placental tissue, combined with the detected EGR1 biological activity indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of developmental anomalies, fetal deficiencies and pre-natal disorders. In addition it may be useful in the detection and

treatment of ovarian and endometrial cancers. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:81 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 694 of SEQ ID NO:81, b is an integer of 15 to 708, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:81, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 72

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:

LAPECCCGSVTYPRALVPRPCCPEPRAPLQLTLGLFSANPVNASPWGRCRSRR GRGNLPLGHPVSTAFSSGDS (SEQ ID NO:388), and/or NTLHSKLVPSVYHSTE KSCLV CFGMCPSIYKKMKSVLLIGTRMLLWLSHISQGPRPEAVLPRAPSP SAAHPWLVFRKPGKRKPLGQMQKQK REGKPASGSPC (SEQ ID NO:389), YPR ALVPRPCCPEPRAPLQLTLGLF (SEQ ID NO:390), and/or VLLIGTRMLL WLSHISQGPRPEAVLPR (SEQ ID NO:391). Polynucleotides encoding these polypeptides are also encompassed by the invention. The gene encoding the disclosed cDNA is believed to reside on chromosome 7. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 7.

This gene is expressed primarily in infant brain, and to a lesser extent, in placenta.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, developmental and neurological disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the developmental and neurological

systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.reproductive, developmental, neural, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:231 as residues: Thr-45 to Arg-50.

The tissue distribution in fetal brain and placenta indicates that polynucleotides and polypeptides corresponding to this gene are useful for the study, diagnosis and treatment of various developmental and neurological disorders and diseases. The protein product of this gene is useful for the detection/treatment of neurodegenerative disease states. behavioural disorders, or inflamatory conditions such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, meningitis, encephalitis. demyelinating diseases, peripheral neuropathies. neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses , autism, and altered bahaviors, including disorders in feeding, sleep patterns, balance, and preception. In addition, elevated expression of this gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or survival. Moreover, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Expression within fetal tissue and other cellular sources marked by proliferating cells indicates that this protein may play a role in the regulation of cellular division, and may show utility in the diagnosis and treatment of cancer and other proliferative disorders. Similarly, developmental tissues rely on decisions involving cell differentiation and/or apoptosis in pattern formation. Thus this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:82 and may have been publicly available prior to conception of the present

invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1450 of SEQ ID NO:82, b is an integer of 15 to 1464, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:82, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 73

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: WIIVMFGKVLKIKDFMSTYSHTYTHTHMHAHTHTHTLTLSLLQNVLTLVAISDS DK ALLIF (SEQ ID NO:392), MTLLIAEKTWRRPWPCQWGYLGAEGDRHLEG RSLSLRHLQGAETPVLNPDLQLPSHIGKQAWSH ALGSL (SEQ ID NO:393), MSTYSHTYTHTHMHAHTHTHTLTLSLL (SEQ ID NO:394), and/or GAEGDRHLE GRSLSLRHLQGAET (SEQ ID NO:395). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in the spleen of patients with lymphocytic leukemia.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, lymphocytic leukemia and other cancers, as well as immune disorders such as AIDS, arthritis and asthma. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in spleen tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of

lymphocytic leukemia and other cancers, as well as other immune disorders and conditions including, AIDS, arthritis, asthma and microbial infection. Furthermore, the protein product of this gene may be useful for the treatment and diagnosis of hematopoetic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:83 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 602 of SEQ ID NO:83, b is an integer of 15 to 616, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:83, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 74

When tested against Jurket and fibroblast cell lines, supernatants removed from cells containing this gene activated both the GAS (gamma activating sequence), and the EGR1 (early growth response gene 1) promoter elements. Thus, it is likely that this gene activates immune or fibroblast cells through the JAK-STAT and/or EGR1 signal transduction pathway. GAS is a promoter element found upstream of many genes which are involved in the Jak-STAT pathway. The Jak-STAT pathway is a large, signal transduction pathway involved in the differentiation and proliferation of cells. Therefore, activation of the Jak-STAT pathway, reflected by the binding of the GAS element, can be used to indicate proteins involved in the proliferation and differentiation

of cells. EGR1 is a separate signal transduction pathway from Jak-STAT, genes containing the EGR1 promoter are induced in various tissues and cell types upon activation, leading the cells to undergo differentiation and proliferation. In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: VVEPGLKASLGA MSTLFPSLFPRVTETLWFNLDRPCVEETELQQQEQQHQAWLQSIAEKDNNLVPI GKPASEHYDDEEEEDD EDDEDSEEDSEDDEDMQDMDEMNDYNESPDDGEVN EVDMEGNEQDQDQWMI (SEQ ID NO:396), LFPRVTETLWFNLDRPCVEETEL (SEQ ID NO:397), and/or YNESPDDGEVNEVDMEGNEQDQD (SEQ ID NO:398). Polynucleotides encoding these polypeptides are also encompassed by the invention. The gene encoding the disclosed cDNA is believed to reside on chromosome 11. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 11.

This gene is expressed primarily in cells of the immune and haemopoietic systems, and to a lesser extent, in several other tissues.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune and haemopoietic disorders, such as multiple myeloma, immunodeficiencies, and inflammatory conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and haemopoietic systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g., cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:233 as residues: Pro-21 to Gly-30.

The tissue distribution in immune tissues and cells, combined with the detected GAS and EGR1 biological acitivity indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatment and diagnosis of disorders of the immune, haemopoietic, and integumentary systems. In addition, polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of hematopoetic related disorders such as anemia, pancytopenia, leukopenia,

thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:84 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 914 of SEQ ID NO:84, b is an integer of 15 to 928, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:84, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 75

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: MGFDIHGVLGEAVAEPREKKQE RAKWAPHDYDDPSLS LQDLLISWMISTWLIPMWKCQATIWFSLIQRLLNAYCMPGNFRHWEIAANTTN KT PGLMDFKFL (SEQ ID NO:399), EPREKKQERAKWAPHDYDDPSLSLQDL (SEQ ID NO:400), and/or MPGNFRHWEIAANTTNKT PGLMDF (SEQ ID NO:401). Polynucleotides encoding these polypeptides are also encompassed by the invention. The gene encoding the disclosed cDNA is believed to reside on the X chromosome. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for the X chromosome.

This gene is expressed primarily in fetal liver and spleen, and to a lesser extent, in prostate cancer and placenta.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a

biological sample and for diagnosis of diseases and conditions which include, but are not limited to, developmental, reproductive, immune, and haemopoietic disorders Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system and developing systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.developmental, hepatic, reproductive, immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g. lymph, amniotic fluid, serum, bile, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in developing and immune tissues indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of disorders of the haemopoietic and developing immune systems. In addition, polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of hematopoetic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Moreover, the expression within fetal tissue and other cellular sources marked by proliferating cells indicates that this protein may play a role in the regulation of cellular division, and may show utility in the diagnosis and treatment of cancer and other proliferative disorders. Similarly, developmental tissues rely on decisions involving cell differentiation and/or apoptosis in pattern formation. Thus this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. The protein may also show utility in the treatment or diagnosis of various hepatic or reproductive disorders, which include, but are not limited to hepatoblastoma, jaundice, hepatitis, liver metabolic diseases and conditions that are attributable to the differentiation of hepatocyte progenitor cells, and prostate cancer, and/or congenital defects such as X-linked conditions. Protein, as well as, antibodies directed against the

protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:85 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 709 of SEQ ID NO:85, b is an integer of 15 to 723, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:85, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 76

This gene is expressed primarily in fetal spleen and Wilm's tumor.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, haemopoietic, immune, developmental, or renal disorders, such as congenital defects, mutliple myeloma, or Wilm's tumor. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the haemopoietic and developing systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.developmental, immune, hematopoietic, renal, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in fetal spleen indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatment and diagnosis of disorders of the haemopoietic and developing systems and cancer. In addition, polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of hematopoetic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the

production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. The expression within embryonic tissue and other cellular sources marked by proliferating cells indicates that this protein may play a role in the regulation of cellular division, and may show utility in the diagnosis and treatment of cancer and other proliferative disorders. Similarly, developmental tissues rely on decisions involving cell differentiation and/or apoptosis in pattern formation. Thus this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:86 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 556 of SEQ ID NO:86, b is an integer of 15 to 570, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:86, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 77

When tested against U937 cell lines, supernatants removed from cells containing this gene activated the (gamma activating sequence) promoter element. Thus, it is likely that this gene activates promyelocytic cells through the JAK-STAT signal transduction pathway. GAS is a promoter element found upstream of many genes which are involved in the Jak-STAT pathway. The Jak-STAT pathway is a large, signal transduction pathway involved in the differentiation and proliferation of cells. Therefore, activation of the Jak-STAT pathway, reflected by the binding of the GAS

element, can be used to indicate proteins involved in the proliferation and differentiation of cells.

This gene is expressed primarily in induced T-cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune and inflammatory diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in T-cells, combined with the detected GAS biological activity indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of immune and inflammatory diseases. The secreted protein can also be used to determine biological activity, to raise antibodies, as tissue markers, to isolate cognate ligands or receptors, to identify agents that modulate their interactions and as nutritional supplements. It may also have a very wide range of biological acitivities. Typical of these are cytokine, cell proliferation/differentiation modulating activity or induction of other cytokines; immunostimulating/immunosuppressant activities (e.g. for treating human immunodeficiency virus infection, cancer, autoimmune diseases and allergy); regulation of hematopoiesis (e.g. for treating anaemia or as adjunct to chemotherapy); stimulation or growth of bone, cartilage, tendons, ligaments and/or nerves (e.g. for treating wounds, stimulation of follicle stimulating hormone (for control of fertility); chemotactic and chemokinetic activities (e.g. for treating infections, tumors); hemostatic or thrombolytic activity (e.g. for treating haemophilia, cardiac infarction etc.); anti-inflammatory activity (e.g. for treating septic shock, Crohn's disease); as antimicrobials; for treating psoriasis or other hyperproliferative diseases; for regulation of metabolism, and behaviour. Also contemplated is the use of the corresponding nucleic acid in gene therapy procedures. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:87 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 625 of SEQ ID NO:87, b is an integer of 15 to 639, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:87, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 78

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: QSVPSPPLAPPLPPSLPSFLFTETRSHYVARLVSNSWAQM ILLPWPLKVLGLDVSHCAWPKSVFLQAMEEIADFCLFSVKYQVSSMTCF DRT SYMKNTYL (SEQ ID NO:402), and/or LFTETRSHYVARLVSNSWAQMILLPWP (SEQ ID NO:403). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in bone marrow.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, anemias (leukemias), immune deficiencies and other hematopoietic-related disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the hematopoietic and immune systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in bone marrow indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of

hematopoietic and immune disorders, which include, but are not limited to the following: leukemias, lymphomas, auto-immunities, immunodeficiencies (e.g. AIDS), immuno-supressive conditions (transplantation) and other hematopoeitic disorders, such as multiple myeloma. In addition this gene product may be applicable in conditions of general microbial infection, inflammation or cancer. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:88 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 694 of SEQ ID NO:88, b is an integer of 15 to 708, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:88, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 79

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:
SQIKSEKKHIGKAYTCTQTQSTGMQSTLTIVAKKKSRNHTESYTRKKQENQIV LIPWHQKKHPEGTHTCSHSLRRDTNTAADTQRKIRAHRYTYRRDKYSDTLVTH DHYKGDKHPSNTHTQPR XEFLQPGGSTNSRAAAPRXSSSFCPFS EGYS SWGYH (SEQ ID NO:404),GMQSTLTIVAKKKSRNHTESYTRKKQ (SEQ ID NO:405), KKHPEGTHTCSHSLRRDTNTAADT (SEQ ID NO:406), and/or RRDKY SDTLVTHDHYKGDKHPSNT (SEQ ID NO:407). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in neutrophils.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune or hematopoietic disorders, such as leukemias, lymphomas, AIDS, arthritis and asthma. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification

of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:238 as residues: Asp-38 to Leu-43.

The tissue distribution in neutrophils indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of immune disorders including leukemias, lymphomas, AIDS, arthritis and asthma, as well as other conditions which potentially implicate the immune system, such as atherosclerosis, cancer and infection. In addition, This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immunodeficiency diseases such as granulomatous disease, inflammatory bowel disease, sepsis, acne, neutropenia, neutrophilia, psoriasis, hypersensitivities, such as T-cell mediated cytotoxicity; immune reactions to transplanted organs and tissues, such as host-versus-graft and graft-versus-host diseases, or autoimmunity disorders, such as autoimmune infertility, lense tissue injury, demyelination, systemic lupus erythematosis, drug induced hemolytic anemia, rheumatoid arthritis, Sjogren's disease, scleroderma and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:89 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more

polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 935 of SEQ ID NO:89, b is an integer of 15 to 949, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:89, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 80

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: KHLPLKAPIDLDNKNSCMFCSRDIFCRFH HSTAWLFL GRITDRILGLHHYLIRYQFEIENLCLMKIVIPVVSMKTNCQFDFLGQLKQNLYH (SEQ ID NO:408), APIDLDNKNSCMFCSRDIFCR (SEQ ID NO:410), and/or IENLCLMKIVIPVVSMKTNCQFDFLGQL (SEQ ID NO:409). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in prostate carcinoma cell line stimulated with 30 nM synthetic androgen, R1881 cells and, to a lesser extent, in activated monocytes.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, reproductive or immune disorders, particularly prostate cancer and prostate ailments. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the prostate, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.immune, reproductive, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, seminal fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in the prostate indicates that polynucleotides and polypeptides corresponding to this gene are useful for the disgnosis and intervention of prostate cancer and prostate ailments, or related proliferative conditions in either said tissue or other tissues. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:90 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1157 of SEQ ID NO:90, b is an integer of 15 to 1171, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:90, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 81

The translation product of this gene shares strong sequence homology with human protocadherin 42 (GenBank accession no. gil387675), PCDH7 (BH-Pcdh)a, and its associated isoforms PCDH7 (BH-Pcdh)b, and PCDH7 (BH-Pcdh)c which are thought to be important in tissue and cell-cell adhesion, repair and development (See Genbank Accession Nos.gnl|PID|d1026122 (AB006755), gnl|PID|d1026123 (AB006756), and gnl|PID|d1026124 (AB006757)). The polynucleotides encoding this gene have been gened by another group subsequent to our filing (See Yoshida K, et al, Genomics 1998 May 1;49(3):458-61, which is hereby incorporated by reference). The cytoplasmic domain of cadherin interacts with the cytoskeleton through catenins and other cytoskeleton associated proteins. The cytoplasmic domain is not present in all cadherins, but in those which possess it, it is essential for the cadherins adhesive function. The cadherins which do not possess a cytoplasmic domain appear to function via a different method from those with a cytoplasmic domain. This protein sequence is involved in cell-cell adhesion. This sequence may have regulatory functions in the cell, as well as the cell-cell adhesive properties. Antibodies produced against this sequence are useful for modulating the binding activity of protocadherins, and can be used therapeutically. BH-Pcdh has an extracellular domain consisting of seven repeats of the cadherin motif (EC 1 to 7). EC2 of BH-Pcdh is unique in having a 55-amino-acid insertion in the middle of the motif. There are three isoforms of BH-Pcdh, denoted -a, -b, and -c, which have different cytoplasmic tails and a 47-amino-acid deletion in the EC2-3 region of BH-Pcdh-c. While only a 9.0-kb message was detected in normal tissues, 4.5- and 9.0-kb mRNA species were seen in the human lung carcinoma cell line A549. Furthermore, only the 4.5-kb mRNA was detected in HeLa cell S3 and

human gastric cancer cell lines MKN28 and KATO-III. Southern blot analysis indicated that the BH-Pcdh gene is likely to be conserved among various vertebrates. In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:

GTSVNESVSNATAIDSQIARSLHIPLTQDIAGDPSYEISKQRLSIVIGVVAGI (SEQ ID NO:411), PKIKMAMKPAKKITKTFLHPNSMTNLKSLKRTRKTKNLSSLSTA ALSLWRLLSQMDRGMIVSMRSCQTAQ AWGDTGPLMVGPAVLTWQGITNL VPHCLLFSFIPSHQLQEKNTRPYKIYHQPTHLWEQETTFQLDQITAL STAVKP ITSTANRCVYIHTLLCLAEFHSNMMLHYAPYCDDLSTPKPAGACPWPWGVSQS LLVPLVVHFIF ESFSFSYTEK (SEQ ID NO:412), CSIMHHTVMTFLLRNLLEPA LGRGVSANHCLFHLLYILFL SLFLSHIQKNSMKIK (SEQ ID NO:413), TAIDS QIARSLHIPLTQDIAGDPSYEISK (SEQ ID NO:414), YCRSKNKNGYEAGKKDH EDFF (SEQ ID NO:415), GPGSPDLARHYKSSSPLPTVQ (SEQ ID NO:416), and/or LPPANTFVGAGDNISIGSDHCSEYS (SEQ ID NO:417). Polynucleotides encoding these polypeptides are also encompassed by the invention. The gene encoding the disclosed cDNA is believed to reside on chromosome 4. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 4.

This gene is expressed primarily in ovarian tumors, and to a lesser extent in, striatum and HL-60 cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, cancer and reproductive dysfunction, in addition to cardiovascular and neural disorders,such as atherosclerosis, and neurodegenerative disorders, such as Alzheimer's and Parkinson's, or other disorders resulting from aberrant cell-adhesion. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproductive, nervous and immune systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.reproductive, neural, cardiovascular, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:240 as residues: Tyr-15 to Leu-59, Ala-68 to Asp-85, Pro-87 to Asn-96, His-120 to Lys-129, Ser-153 to Gln-170.

The tissue distribution in ovarian and muscle tissue, combined with the strong homology to various cadherins indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis, study and treatment of various neoplastic disorders such as squamous cell carcinomas and related tumors, and nervous system and reproductive disorders. Considering the vital importance of cell-adhesion amongst various cellular functions, in particular chemotaxis by the immune and hematopoietic cells indicates that this gene product may play a direct, or in-direct role in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immunodeficiency diseases such as AIDS, leukemia, rheumatoid arthritis, granulomatous disease, inflammatory bowel disease, sepsis, acne, neutropenia, neutrophilia, psoriasis, hypersensitivities, such as T-cell mediated cytotoxicity; immune reactions to transplanted organs and tissues, such as host-versus-graft and graft-versus-host diseases, or autoimmunity disorders, such as autoimmune infertility, lense tissue injury, demyelination, systemic lupus erythematosis, drug induced hemolytic anemia, rheumatoid arthritis, Sjogren's disease, scleroderma and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Furthermore, the secreted protein can also be used to determine biological activity, to raise antibodies, as tissue markers, to isolate cognate ligands or receptors, to identify agents that modulate their interactions and as nutritional supplements. It may also play an in-direct role in the regulation of a very wide range of biological acitivities. Typical of these are cytokine, cell proliferation/differentiation modulating activity or induction of other cytokines; immunostimulating/immunosuppressant activities (e.g. for treating human immunodeficiency virus infection, cancer, autoimmune diseases and allergy); regulation of hematopoiesis (e.g. for treating anaemia or as adjunct to chemotherapy); stimulation or growth of bone, cartilage, tendons, ligaments and/or nerves (e.g. for treating wounds, stimulation of follicle stimulating hormone (for control of fertility); chemotactic and chemokinetic activities (e.g. for treating infections, tumors); hemostatic or thrombolytic activity (e.g. for treating haemophilia, cardiac infarction etc.); anti-

inflammatory activity (e.g. for treating septic shock, Crohn's disease); as antimicrobials; for treating psoriasis or other hyperproliferative diseases; for regulation of metabolism, and behaviour. Also contemplated is the use of the corresponding nucleic acid in gene therapy procedures. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:91 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1137 of SEQ ID NO:91, b is an integer of 15 to 1151, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:91, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 82

The translation product of this gene shares sequence homology with the G-protein coupled receptor TM3 consensus polypeptide which may implicate an important function for this protein in various signal transduction pathways. G-protein coupled receptors are known to have a variety of functions including modulating immune system tissue through interaction with cytokines and lymphokines. In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:

GTSNASVSPTICICMCGYVHIWFFICLCVYLKVLQGSACPWIAAAVVMRRMRK VQEKGEVFRNMAATWAL RSGIQSLNSLVSSAFFTIFMTLGSSWNLIVSLSSLV NWTGLFSFYFSRN (SEQ ID NO:418), CLCVYLKVLQGSACPWIAAAVV MRRMRK (SEQ ID NO:419), and/or TIFMTLGSSWNLIVSLSSLVNWTGLF (SEQ ID NO:420). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in breast lymph node.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are

not limited to, breast cancer, or other immune or reproductive disorders and diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.immune, reproductive, breast, cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, breast milk, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:241 as residues: Cys-34 to Gly-48.

The tissue distribution in breast lymph nodes and homology to a conserved G-protein coupled receptor TM3 consensus sequence indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment for breast cancer or immune diseases. Considering the vast roles which G-protein coupled receptors play in the maintenance of important cellular fuctions, the secreted protein may have a very wide range of biological acitivities. Typical of these are cytokine, cell proliferation/differentiation modulating activity or induction of other cytokines; immunostimulating/immunosuppressant activities (e.g. for treating human immunodeficiency virus infection, cancer, autoimmune diseases and allergy); regulation of hematopoiesis (e.g. for treating anaemia or as adjunct to chemotherapy); stimulation or growth of bone, cartilage, tendons, ligaments and/or nerves (e.g. for treating wounds, stimulation of follicle stimulating hormone (for control of fertility); chemotactic and chemokinetic activities (e.g. for treating infections, tumors); hemostatic or thrombolytic activity (e.g. for treating haemophilia, cardiac infarction etc.); anti-inflammatory activity (e.g. for treating septic shock, Crohn's disease); as antimicrobials; for treating psoriasis or other hyperproliferative diseases; for regulation of metabolism, and behaviour. Also contemplated is the use of the corresponding nucleic acid in gene therapy procedures. Furthermore, the protein may also be used to determine biological activity, to raise antibodies, as tissue markers, to isolate cognate ligands or receptors, to identify agents that modulate their interactions and as nutritional supplements.Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ

ID NO:92 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 700 of SEQ ID NO:92, b is an integer of 15 to 714, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:92, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 83

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:

QPDIPVLPVGFSQNCSFKVSGCWKGGLIAEKVGTLGTPKGRR AWPETEF FRFLEPGLP (SEQ ID NO:421), and/or RGFRMAQPLVNTFQVAVPVEDL APQQNPSRFPADPALLSFLTG SILAPGKVIWVNVSFTAIIWPTWDSMAI GELTIASHASMTLHIGRPGSRKRKNSVSGHARLPFGVPSVPT FSAISPP FQQPETLKEQF (SEQ ID NO:422), EDLAPQQNPSRFPADPALLSFLTG (SEQ ID NO:423), and/or TWDSMAIGELTIASHASMTLHIGRPGSRK (SEQ ID NO:424). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in activated T-cells, hepatocellular tumor, pancreas islet cell tumors, and hemangiopericytoma.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune, hepatic, and endocrine disorders, such as cancers, particularly of T-cells, hepatocellular tumors and pancreas islet cell tumors. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.immune, hepatic, endocrine, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, bile, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:242 as residues: Glu-43 to Lys-50, Ser-53 to Phe-60.

The tissue distribution in T-cells, hepatocellular tumors, and pancreatic islet cell tumors indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and intervention of immune, hepatic, and endocrine disorders, and other cancer types. Expression within cellular sources marked by proliferating cells indicates that this protein may play a role in the regulation of cellular division, and may show utility in the diagnosis and treatment of cancer and other proliferative disorders in various tissues, aside from those disclosed above. Similarly, developmental tissues rely on decisions involving cell differentiation and/or apoptosis in pattern formation. Thus this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:93 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 796 of SEQ ID NO:93, b is an integer of 15 to 810, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:93, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 84

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:

VSPQLMGIKREPSAAQLSVGEEHTLDREGRELVDLPGQPSQKIKIKNKSSLHPG LIIPP AHYKTATTTNLF (SEQ ID NO:425), and/or PSAAQLSVGEEHTLDREGREL (SEQ ID NO:426). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in hepatocellular tumors.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a

biological sample and for diagnosis of diseases and conditions which include, but are not limited to, hepatic disorders, such as liver diseases and hepatocellular tumor, including proliferative disorders in other tissues and cell types. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the hepatic system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.hepatic, proliferating, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, bile, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in hepatocellular tumor tissues indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and intervention of hepatocellular tumor or other liver disorders. Specifically, polynucleotides and polypeptides corresponding to this gene are useful for the detection and treatment of liver disorders and cancers (e.g. hepatoblastoma, jaundice, hepatitis, liver metabolic diseases and conditions that are attributable to the differentiation of hepatocyte progenitor cells). Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:94 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1162 of SEQ ID NO:94, b is an integer of 15 to 1176, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:94, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 85

When tested against reh cell lines, supernatants removed from cells containing this gene activated the GAS (gamma activating sequence) promoter element. Thus, it is

likely that this gene activates B-cells through the JAK-STAT signal transduction pathway. GAS is a promoter element found upstream of many genes which are involved in the Jak-STAT pathway. The Jak-STAT pathway is a large, signal transduction pathway involved in the differentiation and proliferation of cells. Therefore, activation of the Jak-STAT pathway, reflected by the binding of the GAS element, can be used to indicate proteins involved in the proliferation and differentiation of cells. In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: NCDHDFIQPLHTPMSAL FQSEFS (SEQ ID NO:427), SILNM GLFTEQRPWPAAARCARQSTVAGAIRRARGTVTMWQVAGAAW ASPDRRAKV HPCRHAAPCLPSPCRRGLQMSGPLQATRGRVTLRSHQVGCKRATGSIENSL (SEQ ID NO:428), QKSKGSPLQTCCSLPTLPMQERPADEWSTPGDQGKSYIK KPPGGLQKGHRLHRKLTLKQGRHRGVE GLNEIMVTVLKEEFPVSKPGLNV LPTFHRHHECYQHGMNLTARISVVS (SEQ ID NO:429), ARQSTVAGAIRR ARGTVTMWQVAGA (SEQ ID NO:430), PCRRGLQMSGPLQATRGRVTLRSHQ (SEQ ID NO:431), LPMQERPADEWSTPGDQGKSYIKKPP (SEQ ID NO:432), and/or NVLPTFHRHHECYQHGMNLTARI (SEQ ID NO:433). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in human fetal kidney, adult testis, T-cell lymphoma, and a fetal liver/spleen cDNA library.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, renal, developmental, reproductive, immune, or hematopoietic disorders, particularly kidney disease, lymphoma, congenital defects, multiple myeloma, SCID, male sterility, and cancers. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the kidney and immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.immune, hematopoeitic, reproductive, renal, developmental, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:244 as residues: Gly-35 to Gly-40.

The tissue distribution in fetal kidney and T-cells, combined with the detected GAS biological activity indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis or treatement of kidney diseases or immune disorders, especially cancers. Specifically, this gene or gene product could be used in the treatment and/or detection of kidney diseases including renal failure, nephritus, renal tubular acidosis, proteinuria, pyuria, edema, pyelonephritis, hydronephritis, nephrotic syndrome, crush syndrome, glomerulonephritis, hematuria, renal colic and kidney stones, in addition to Wilms Tumor Disease, and congenital kidney abnormalities such as horseshoe kidney, polycystic kidney, and Falconi's syndrome. Expression within fetal tissue and other cellular sources marked by proliferating cells indicates that this protein may play a role in the regulation of cellular division, and may show utility in the diagnosis and treatment of cancer and other proliferative disorders. Similarly, developmental tissues rely on decisions involving cell differentiation and/or apoptosis in pattern formation. Thus this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:95 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1014 of SEQ ID NO:95, b is an integer of 15 to 1028, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:95, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 86

When tested against U937 cell lines, supernatants removed from cells containing this gene activated the GAS (gamma activating sequence) promoter element. Thus, it is likely that this gene activates promyelocytic cells through the JAK-STAT signal transduction pathway. GAS is a promoter element found upstream of many genes which are involved in the Jak-STAT pathway. The Jak-STAT pathway is a large, signal transduction pathway involved in the differentiation and proliferation of cells.

Therefore, activation of the Jak-STAT pathway, reflected by the binding of the GAS element, can be used to indicate proteins involved in the proliferation and differentiation of cells.

This gene is expressed primarily in breast, human embryo, and chronic spleen lymphocytic leukemia.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, reproductive, developmental, hematopoietic or immune disorders, such as breast cancer, congenital birth defects, or leukemia. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the breast or hematopoietic systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.reproductive, immune, hematopoietic, developmental, breast, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, amniotic fluid, breast milk, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:245 as residues: His-2 to Asn-8, Gln-35 to Phe-44.

The tissue distribution in breast and lymphocytic leukemia cells, combined with the detected GAS biological activity indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis or intervention of breast cancer, leukemia or other hematopoietic related disorders. Moreover, polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of hematopoetic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies

directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:96 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 733 of SEQ ID NO:96, b is an integer of 15 to 747, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:96, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 87

This gene is expressed primarily in brain containing medulla blastoma.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neural disorders, particularly specific brain tumors such as medulla blastoma, as well as other diseases and conditions of the brain, such as schizophrenia, Alzheimer's disease, Tourette's syndrome, Parkinson's disease, Huntington's disease, mania, dementia, paranoia, depressive and addictive predispositions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.neural, cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in brain tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of specific brain tumors such as medulla blastoma. In addition it may also be useful for the diagnosis and treatment of developmental, degenerative and behavioral conditions of the

brain and nervous system, such as schizophrenia, Alzheimer's disease, Parkinson's disease, Huntington's disease, Tourette's syndrome, mania, dementia, paranoia, addictive behavior, obsessive-compulsive and sleep disorders. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:97 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 614 of SEQ ID NO:97, b is an integer of 15 to 628, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:97, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 88

When tested against Jurket cell lines, supernatants removed from cells containing this gene activated the GAS (gamma activating sequence) promoter element. Thus, it is likely that this gene activates T-cells through the JAK-STAT signal transduction pathway. GAS is a promoter element found upstream of many genes which are involved in the Jak-STAT pathway. The Jak-STAT pathway is a large, signal transduction pathway involved in the differentiation and proliferation of cells. Therefore, activation of the Jak-STAT pathway, reflected by the binding of the GAS element, can be used to indicate proteins involved in the proliferation and differentiation of cells. In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: INVLYCSRDSLMGRTIMESSDYIKKGANVSPVLGVRQQ AV (SEQ ID NO:434). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in adrenal gland tumor and T-cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, diseases of the endocrine and immune or haemopoietic systems, particularly inflammatory or immunodeficiency conditions, such as AIDS. Similarly,

polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and endocrine systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.immune, hematopoietic, endocrine, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in T-cells and adrenal gland tissues, combined with the detected GAS biological activitiy indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatment and diagnosis of disorders of the immune and endocrine systems and cancer. Moreover, the secreted protein can also be used to determine biological activity, to raise antibodies, as tissue markers, to isolate cognate ligands or receptors, to identify agents that modulate their interactions and as nutritional supplements. It may also have a very wide range of biological acitivities. Typical of these are cytokine, cell proliferation/differentiation modulating activity or induction of other cytokines; immunostimulating/immunosuppressant activities (e.g. for treating human immunodeficiency virus infection, cancer, autoimmune diseases and allergy); regulation of hematopoiesis (e.g. for treating anaemia or as adjunct to chemotherapy); stimulation or growth of bone, cartilage, tendons, ligaments and/or nerves (e.g. for treating wounds, stimulation of follicle stimulating hormone (for control of fertility); chemotactic and chemokinetic activities (e.g. for treating infections, tumors); hemostatic or thrombolytic activity (e.g. for treating haemophilia, cardiac infarction etc.); anti-inflammatory activity (e.g. for treating septic shock, Crohn's disease); as antimicrobials; for treating psoriasis or other hyperproliferative diseases; for regulation of metabolism, and behaviour. Also contemplated is the use of the corresponding nucleic acid in gene therapy procedures. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:98 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more

polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 890 of SEQ ID NO:98, b is an integer of 15 to 904, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:98, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 89

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: SLLMYFVFKIFFQSLCVLGYCILPLTVA (SEQ ID NO:435). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in dendritic cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.immune, cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual.having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:248 as residues: Thr-43 to Thr-48.

The tissue distribution in dendritic cells indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of immune system disorders. In addition, polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of hematopoetic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product

may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:99 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 562 of SEQ ID NO:99, b is an integer of 15 to 576, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:99, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 90

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:
RLWMTKAHPALRHLLLLFTLALTLLAQGCCAVAPSGCADLAGFCSLGHS C (SEQ ID NO:436). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in human stomach.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, digestive and gastrointestinal conditions, particularly ulcers and cancers. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the gastrointestinal system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.gastrointestinal, metabolic, mucosal, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, chyme, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression

level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:249 as residues: Pro-32 to Gly-38.

The tissue distribution in stomach tissues indicates that polynucleotides and polypeptides corresponding to this gene are useful for the study and treatment of gastrointestinal disorders, or other disorders afflicting mucosal or endothelial tissues. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:100 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 699 of SEQ ID NO:100, b is an integer of 15 to 713, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:100, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 91

The translation product of this gene was found to have homology to the conserved K07F5.14 protein from Caenorhabditis elegans (See Genbank Accession No gnl|PID|e233697) which may be important in regulation of important cellular functions, including homeostasis and cell division. When tested against U937 cell lines, supernatants removed from cells containing this gene activated the GAS (gamma activating sequence) pathway. Thus, it is likely that this gene activates promyelocytic cells through the JAK-STAT signal transduction pathway. GAS is a promoter element found upstream of many genes which are involved in the Jak-STAT pathway. The Jak-STAT pathway is a large, signal transduction pathway involved in the differentiation and proliferation of cells. Therefore, activation of the Jak-STAT pathway, reflected by the binding of the GAS element, can be used to indicate proteins involved in the proliferation and differentiation of cells. In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:
RTCTPWMGFWCLVCSLFAPVPTSRKYLVSKPGCYQRRRV FGVCFTKPL (SEQ

ID NO:437), WLLSEKKG (SEQ ID NO:438), and/or GVFYKAAVIG (SEQ ID NO:439). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in bone marrow and T cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune or hematopoietic disorders, particularly multiple myeloma, immunodeficiencies, and cancers. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and endocrine systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in bone marrow and T-cells, combined with the detected GAS biological activity in U937 cells indicates that polynucleotides and polypeptides corresponding to this gene are useful for study and treatment of immune and hormonal disorders and neoplasias. Specifically, polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of hematopoetic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Moreover, the protein may be also used as an agent for immunological disorders including arthritis, asthma, immunodeficiency diseases such as AIDS, leukemia, rheumatoid arthritis, granulomatous disease, inflammatory bowel disease, sepsis, acne, neutropenia, neutrophilia, psoriasis, hypersensitivities, such as T-cell mediated cytotoxicity; immune reactions to transplanted organs and tissues, such as host-versus-graft and graft-versus-host diseases, or autoimmunity disorders, such as autoimmune

infertility, lense tissue injury, demyelination, systemic lupus erythematosis, drug induced hemolytic anemia, rheumatoid arthritis, Sjogren's disease, scleroderma and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:101 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 635 of SEQ ID NO:101, b is an integer of 15 to 649, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:101, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 92

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: CKTSPLPKEGQSAVSVPVSSHFLAHSAPLSGGHAHVFARDGATGL (SEQ ID NO:440), LGRGSGERKTPVSCFAQISKSRGGRSKSLTHLCTHTHTQVTEL DVRMSHGCLRXQHAGRLAPPPPLRFCL TACWGRRGEAETVWKDPASSQ HPPPSEKPHRQDRHPERWHQPGGPIPGKHMRVSPGQRGRVCQEMGRNRN (SEQ ID NO:441), FCLRDFKIWRGRLEAGRTEGRL AGERFGGEEDPSFLFC SDFKVEGWAFEISHSLVHTHTHTGHGAGRADVTRVPAGTARWEAGSPTPSPV LF DSLLGAAGRG (SEQ ID NO:442), AQISKSRGGRSKSLTHLCTHTHTQVTEL (SEQ ID NO:443), EKPHRQDRHPERWHQPGGPIPGKHMR (SEQ ID NO:444), GRLEAGRTEGRL AGERFGGEEDPSFL (SEQ ID NO:445), and/or VTRVPAGTARWEAGSPTPSPVLF (SEQ ID NO:446). Polynucleotides encoding these polypeptides are also encompassed by the invention.The gene encoding the disclosed cDNA is believed to reside on chromosome 19. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 19.

This gene is expressed primarily in ovary, spinal cord, and fetal spleen.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, developmental, reproductive, and neurological conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the nrevous and reproductive systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.developmental, reproductive, ovarian, immune, hematopoeitic, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:251 as residues: Pro-34 to Pro-53.

The tissue distribution in spinal cord and fetal spleen indicates that polynucleotides and polypeptides corresponding to this gene are useful for the study and treatment of neural, hematopoietic, and developmental disorders. Specifically, polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states, behavioural disorders, or inflamatory conditions such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, meningitis, encephalitis, demyelinating diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses , autism, and altered bahaviors, including disorders in feeding, sleep patterns, balance, and preception. In addition, elevated expression of this gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or survival.Moreover, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Moreover, polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of hematopoetic related disorders such as anemia, pancytopenia,

leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include, but are not limited to bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:102 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 683 of SEQ ID NO:102, b is an integer of 15 to 697, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:102, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 93

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: DEGVQGERLFRILRINGEKPYNFVDYFHCEY (SEQ ID NO:447), KVVRIDNGILCSHKKTEIMSLQQHGWIWRPYLKQTNTGTENQIPHTL TYKWELNFEYIXTQXRGXXDSEAYLKVEGGRREGIQKLPIRYYVYYLGDKIICT SSSCSMHLLM (SEQ ID NO:448), HKDTCMSMFT AALFTIAKTWN (SEQ ID NO:449), MPINDRLDFKRWYV (SEQ ID NO:450), TMESYVAIKRQRSCPCSNM VGSGGHILSKLTQEQKTKYHILS LISGS (SEQ ID NO:451), EIMSLQQHGWIW RPYLKQTNTGTEN (SEQ ID NO:452), and/or RREGIQKLPIRYYVYYLGDKIICT (SEQ ID NO:453). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in bladder tissue from a human male.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, gastrointestinal, urogenital, and nephrotic conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a

number of disorders of the above tissues or cells, particularly of the gastrointestinal and excretory systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.renal, bladder, cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:252 as residues: Arg-52 to Ala-57, Pro-66 to Thr-72.

The tissue distribution in bladder tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for study and treatment of gastrointestinal and urinary tract disorders.Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:103 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1274 of SEQ ID NO:103, b is an integer of 15 to 1288, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:103, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 94

This gene is expressed primarily in bladder tissue from a human male.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, gastrointestinal, renal, and urinary tract conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the intestinal and urinary tract, expression of this gene at significantly higher or lower levels may be

detected in certain tissues or cell types (e.g.renal, urogenital, bladder, cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in bladder tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for study and treatment of urinary tract and gastrointestinal disorders. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:104 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1013 of SEQ ID NO:104, b is an integer of 15 to 1027, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:104, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 95

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: LHGEQVPI YIFLLMQPLNFECISFLNCIEQYSVGVI HNSV TIYACDREENCMDIRYL (SEQ ID NO:454), and/or GTSWASRFFTCH (SEQ ID NO:455). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in T-cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune and inflammatory disorders, particularly immunodeficiencies such as AIDS. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of

the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:254 as residues: Lys-28 to Thr-34.

The tissue distribution in T-cells indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatment and diagnosis of disorders of the immune system. Moreover, This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immunodeficiency diseases such as AIDS, leukemia, rheumatoid arthritis, granulomatous disease, inflammatory bowel disease, sepsis, acne, neutropenia, neutrophilia, psoriasis, hypersensitivities, such as T-cell mediated cytotoxicity; immune reactions to transplanted organs and tissues, such as host-versus-graft and graft-versus-host diseases, or autoimmunity disorders, such as autoimmune infertility, lense tissue injury, demyelination, systemic lupus erythematosis, drug induced hemolytic anemia, rheumatoid arthritis, Sjogren's disease, scleroderma and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:105 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 696 of SEQ ID NO:105, b is an integer of 15 to 710, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:105, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 96

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: GPPRXFXPKKAILGXPPXGRVPPFRYRSRNSRGRPHXSAPRVRFCLENSWLR (SEQ ID NO:456), and/or PLNTMMCMMCKMKVSPKIFSKLKRKYLNSNTLTKL EMQTVHLESSLASCSPNKSGXVGRTR GVDPGNSGTGT (SEQ ID NO:457). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in lymphoma and frontal cortex.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neurological and haemopoietic diseases, particularly neurodegenerative conditions such as Alzheimers and Parkinsons. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and neural systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.neural, immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in frontal cortex and lymphoma indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatment and diagnosis of diseases of the neural and haemopoietic systems. Specifically, polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states, behavioural disorders, or inflamatory conditions such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, meningitis, encephalitis, demyelinating diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses , autism, and altered bahaviors, including disorders in feeding, sleep patterns, balance, and preception. In addition, elevated expression of this

gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or survival.Moreover, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Moreover, the expression within cellular sources marked by proliferating cells indicates that this protein may play a role in the regulation of cellular division, and may show utility in the diagnosis and treatment of cancer and other proliferative disorders. Since, developmental tissues rely on decisions involving cell differentiation and/or apoptosis in pattern formation, this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:106 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 516 of SEQ ID NO:106, b is an integer of 15 to 530, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:106, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 97

This gene is expressed primarily in the spleen of a patient with metastatic melanoma.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune or hematopoietic disorders, particularly metastatic melanoma and other cancers, as well as immune disorders and conditions such as anemias, AIDS,

arthritis and asthma. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g., immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:256 as residues: Pro-26 to Asn-34.

The tissue distribution in spleen indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of metastatic melanomas and other cancers, as well as other immune disorders and conditions including leukemias, lymphomas, AIDS, arthritis, asthma and microbial infection. Furthermore, polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of hematopoetic related disorders such as anemia, pancytopenia, leukopenia, or thrombocytopenia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:107 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 378 of SEQ ID NO:107, b is an integer of 15

to 392, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:107, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 98

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: GTVTQKRK CVFGKYLLSTCSLMFSSMHGACSWKA KQTSSSAGFLCLHVLCPALQLTREKYKTWPWPSFI (SEQ ID NO:458), and/or MKEGQGHVLYF SRVNCKAGHXTCRQRKPADELVCFAFQEQAPCILLNI RLQVLNKYLPNTHFLFCVTVP (SEQ ID NO:459). Polynucleotides encoding these polypeptides are also encompassed by the invention. The gene encoding the disclosed cDNA is believed to reside on chromosome 8. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 8.

This gene is expressed primarily in pineal gland and synovial sarcoma.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, endocrine or skeletal disorders, including cancers. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the endocrine system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.endocrine, pineal, skeletal, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in pineal gland indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatment and diagnosis of disorders of the endocrine system. In addition, polynucleotides and polypeptides corresponding to this gene are useful for the detection, treatment, and/or prevention of various endocrine disorders and cancers, particularly Addison's disease, Cushing's Syndrome, and disorders and/or cancers of the pancrease (e.g. diabetes mellitus), adrenal cortex, ovaries, pituitary (e.g., hyper-, hypopituitarism), thyroid (e.g. hyper-, hypothyroidism), parathyroid (e.g. hyper-,hypoparathyroidism) , hypothallamus, and testes. Alternatively, the expression of this gene product in synovium would suggest a

role in the detection and treatment of disorders and conditions affecting the skeletal system, in particular osteoporosis, bone cancer, as well as, disorders afflicting connective tissues (e.g. arthritis, trauma, tendonitis, chrondomalacia and inflammation), such as in the diagnosis or treatment of various autoimmune disorders such as rheumatoid arthritis, lupus, scleroderma, and dermatomyositis as well as dwarfism, spinal deformation, and specific joint abnormalities as well as chondrodysplasias (ie. spondyloepiphyseal dysplasia congenita, familial osteoarthritis, Atelosteogenesis type II, metaphyseal chondrodysplasia type Schmid). Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:108 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 977 of SEQ ID NO:108, b is an integer of 15 to 991, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:108, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 99

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: TMTGIDSSPEEILRQVGCKQQQGKGVEHVEGSSAEAGEAARGGGAK GGGG AAGKGTSKVGTLRRTRGST (SEQ ID NO:460). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in breast and fetal spleen.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, diseases of the reproductive system and developing organs, particularly congenital defects afflicting the immune or hematopoietic system, such as immunodeficiencies. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification

of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the developing and reproductive systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.reproductive, developing, immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:258 as residues: Gly-23 to Asn-30, Ser-37 to Asn-43.

The tissue distribution in fetal spleen indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatment and diagnosis of diseases involving developmental tissues and reproductive organs. The secreted protein can also be used to determine biological activity, to raise antibodies, as tissue markers, to isolate cognate ligands or receptors, to identify agents that modulate their interactions and as nutritional supplements. It may also have a very wide range of biological acitivities. Typical of these are cytokine, cell proliferation/differentiation modulating activity or induction of other cytokines; immunostimulating/immunosuppressant activities (e.g. for treating human immunodeficiency virus infection, cancer, autoimmune diseases and allergy); regulation of hematopoiesis (e.g. for treating anaemia or as adjunct to chemotherapy); stimulation or growth of bone, cartilage, tendons, ligaments and/or nerves (e.g. for treating wounds, stimulation of follicle stimulating hormone (for control of fertility); chemotactic and chemokinetic activities (e.g. for treating infections, tumors); hemostatic or thrombolytic activity (e.g. for treating haemophilia, cardiac infarction etc.); anti-inflammatory activity (e.g. for treating septic shock, Crohn's disease); as antimicrobials; for treating psoriasis or other hyperproliferative diseases; for regulation of metabolism, and behaviour. Also contemplated is the use of the corresponding nucleic acid in gene therapy procedures. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:109 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of

a-b, where a is any integer between 1 to 898 of SEQ ID NO:109, b is an integer of 15 to 912, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:109, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 100

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:

AQREAGSRPRRRKSLKAVAMLXVEMGGGCRGSMGPGPGYSAGSRVCRGSSL PQVAPFNPSRAHLLPPPVG GGLNSVWLSGVQLSTPPYADWEGVGQSPQ PRGPWMGSSSLGTVGPGCVLSGCPTVKANGGSPCSEMLGER RLLEPSVG PVSGCPERREGGHGARGAAGVVVKGHASVQLNFLSLI (SEQ ID NO:461), KAEFTFAKEKNAKAQLGKKGTRWVKHDKRKEIQLYGCVTLNDDPSCPPCPVP TLPPFWTA TYGSHGRFQKPPFSQHLRAGGAPVGLDCGAPTQYAARPHGPK (SEQ ID NO:462), GCRGSMGPGPGYSAGSRVCRGSSLPQ (SEQ ID NO:463), QPRGPWMGSSSLGTVGPGCVLS (SEQ ID NO:464), and/or GAAGVVVKGH ASVQLNFLSLI (SEQ ID NO:465). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in endothelial, immune, and cancer cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, diseases involving immune, endothelial, and haemopoietic tissues or cells, particularly cancers, inflammatory or immunodeficiency conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune, haemopoietic and endothelial systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.endothelial, immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in immune and hematopoietic tissues indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis

and treatment of disorders of the immune and haemopoietic systems, including cancer. More specifically, this gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immunodeficiency diseases such as AIDS, leukemia, rheumatoid arthritis, granulomatous disease, inflammatory bowel disease, sepsis, acne, neutropenia, neutrophilia, psoriasis, hypersensitivities, such as T-cell mediated cytotoxicity; immune reactions to transplanted organs and tissues, such as host-versus-graft and graft-versus-host diseases, or autoimmunity disorders, such as autoimmune infertility, lense tissue injury, demyelination, systemic lupus erythematosis, drug induced hemolytic anemia, rheumatoid arthritis, Sjogren's disease, scleroderma and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:110 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 861 of SEQ ID NO:110, b is an integer of 15 to 875, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:110, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 101

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: GKPLSAIFPICH MMFLPGKFNLGISHRCCRMT SPWDK RQQLRQECKSDPHVQNPRIHFPESKNSFPSAYIFVSEGNGVSPSK WHCIY SGTSLSH (SEQ ID NO:466), and/or GERGRYQSKYSATWMVTPHYLQTQRC

KLREMNSWIQGNEFLDSEHEGQIYIPVSIVDAYPKD (SEQ ID NO:467). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in human kidney, and to a lesser extent, in liver.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, kidney, urogenital, hepatic, and endocrine disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the renal or endocrine systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.urogenital, kidney, endocrine, hepatic, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, bile, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:260 as residues: Glu-38 to Lys-43.

The tissue distribution in kidney indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of renal disorders, including noninflammatory and inflammatory lesions, and tumors of the kidney. Moreover,this gene or gene product could be used in the treatment and/or detection of kidney diseases including renal failure, nephritus, renal tubular acidosis, proteinuria, pyuria, edema, pyelonephritis, hydronephritis, nephrotic syndrome, crush syndrome, glomerulonephritis, hematuria, renal colic and kidney stones, in addition to Wilms Tumor Disease, and congenital kidney abnormalities such as horseshoe kidney, polycystic kidney, and Falconi's syndrome. Alternatively, expression within liver indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection and treatment of liver disorders and cancers (e.g. hepatoblastoma, jaundice, hepatitis, liver metabolic diseases and conditions that are attributable to the differentiation of hepatocyte progenitor cells). Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ

ID NO:111 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 445 of SEQ ID NO:111, b is an integer of 15 to 459, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:111, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 102

This gene is expressed primarily in kidney cortex and fetal tissue.utility_

The tissue distribution in kidney indicates that this gene or gene product could be used in the treatment and/or detection of kidney diseases including renal failure, nephritus, renal tubular acidosis, proteinuria, pyuria, edema, pyelonephritis, hydronephritis, nephrotic syndrome, crush syndrome, glomerulonephritis, hematuria, renal colic and kidney stones, in addition to Wilms Tumor Disease, and congenital kidney abnormalities such as horseshoe kidney, polycystic kidney, and Falconi's syndrome. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:112 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 595 of SEQ ID NO:112, b is an integer of 15 to 609, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:112, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 103

This gene is expressed primarily in ovary and brain.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, reproductive and neurological conditions, particularly proliferative disorders, such as ovarian cysts or cancer, in addition to neurodegenerative conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the nervous and immune systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.neural, reproductive, endocrine, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in ovarian tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for study and treatment of reproductive disorders, such as infertility. Alternatively, polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states, behavioural disorders, or inflamatory conditions such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, meningitis, encephalitis, demyelinating diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses , autism, and altered bahaviors, including disorders in feeding, sleep patterns, balance, and preception. In addition, elevated expression of this gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or survival.Moreover, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:113 and may have been publicly available prior to conception of the present

invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1390 of SEQ ID NO:113, b is an integer of 15 to 1404, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:113, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 104

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: ISIRGRIL YKMAYFKVCVIIWFQQFCVEETSIIKNVRMLTSEFQNSYATPVSGLLPGAVAWR GGAVYGWVRHAMQVLQ KEPTQPSSFLPPSDAASFWGPESRLHLTW (SEQ ID NO:468), KPFAFSARNFPTMLSEAYFQDPRMRQHHLGVERMTV AWVPSAIP AWRASPTRTQHHPSKPQHQEGAQKQGWHMNSGILMSAYEHFL (SEQ ID NO:469), and/or HSKQNICREVNILKMFLHEIKKTVTDNISTQRRFTYNHQPGS VSIFSVTDILDFEVPFGL (SEQ ID NO:470). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in melanocytes, and PHA stimulated T cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune or integumentary system disorders, and cancers. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.integumentary, immune, hematopoieitc, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in immune cells indicates that polynucleotides and polypeptides corresponding to this gene are useful for study, diagnosis and treatment of cancers and immune system disorders. Alernatively, the expression in melanocytes

indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment, diagnosis, and/or prevention of various skin disorders including congenital disorders (i.e. nevi, moles, freckles, Mongolian spots, hemangiomas, port-wine syndrome), integumentary tumors (i.e. keratoses, Bowen's disease, basal cell carcinoma, squamous cell carcinoma, malignant melanoma, Paget's disease, mycosis fungoides, and Kaposi's sarcoma), injuries and inflammation of the skin (i.e.wounds, rashes, prickly heat disorder, psoriasis, dermatitis), atherosclerosis, uticaria, eczema, photosensitivity, autoimmune disorders (i.e. lupus erythematosus, vitiligo, dermatomyositis, morphea, scleroderma, pemphigoid, and pemphigus), keloids, striae, erythema, petechiae, purpura, and xanthelasma. In addition, such disorders may predispose increased susceptibility to viral and bacterial infections of the skin (i.e. cold sores, warts, chickenpox, molluscum contagiosum, herpes zoster, boils, cellulitis, erysipelas, impetigo, tinea, althletes foot, and ringworm). Moreover, the protein product of this gene may also be useful for the treatment or diagnosis of various connective tissue disorders such as arthritis, trauma, tendonitis, chrondomalacia and inflammation, autoimmune disorders such as rheumatoid arthritis, lupus, scleroderma, and dermatomyositis as well as dwarfism, spinal deformation, and specific joint abnormalities as well as chondrodysplasias (ie. spondyloepiphyseal dysplasia congenita, familial osteoarthritis, Atelosteogenesis type II, metaphyseal chondrodysplasia type Schmid). Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:114 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 839 of SEQ ID NO:114, b is an integer of 15 to 853, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:114, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 105

This gene is expressed primarily in B cell lymphoma, and to a lesser extent, in dermal fibrosarcoma.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune or integumentary disorders, particularly lymphatic and soft tissue cancers. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.immune, hematopoietic, integumentary, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in B-cell lymphoma indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of hematopoetic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Alternatively, the protein product of this gene may also be useful for the treatment, diagnosis, and/or prevention of various skin disorders including congenital disorders (i.e. nevi, moles, freckles, Mongolian spots, hemangiomas, port-wine syndrome), integumentary tumors (i.e. keratoses, Bowen's disease, basal cell carcinoma, squamous cell carcinoma, malignant melanoma, Paget's disease, mycosis fungoides, and Kaposi's sarcoma), injuries and inflammation of the skin (i.e.wounds, rashes, prickly heat disorder, psoriasis, dermatitis), atherosclerosis, uticaria, eczema, photosensitivity, autoimmune disorders (i.e. lupus erythematosus, vitiligo, dermatomyositis, morphea, scleroderma, pemphigoid, and pemphigus), keloids, striae, erythema, petechiae, purpura, and xanthelasma. In addition, such disorders may predispose increased susceptibility to

viral and bacterial infections of the skin (i.e. cold sores, warts, chickenpox, molluscum contagiosum, herpes zoster, boils, cellulitis, erysipelas, impetigo, tinea, althletes foot, and ringworm). Moreover, the protein product of this gene may also be useful for the treatment or diagnosis of various connective tissue disorders such as arthritis, trauma, tendonitis, chrondomalacia and inflammation, autoimmune disorders such as rheumatoid arthritis, lupus, scleroderma, and dermatomyositis as well as dwarfism, spinal deformation, and specific joint abnormalities as well as chondrodysplasias (ie. spondyloepiphyseal dysplasia congenita, familial osteoarthritis, Atelosteogenesis type II, metaphyseal chondrodysplasia type Schmid). Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:115 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 831 of SEQ ID NO:115, b is an integer of 15 to 845, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:115, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 106

When tested against U937 cell lines, supernatants removed from cells containing this gene activated the GAS (gamma activating sequence) promoter element. Thus, it is likely that this gene activates promyelocytic cells through the JAK-STAT signal transduction pathway. GAS is a promoter element found upstream of many genes which are involved in the Jak-STAT pathway. The Jak-STAT pathway is a large, signal transduction pathway involved in the differentiation and proliferation of cells. Therefore, activation of the Jak-STAT pathway, reflected by the binding of the GAS element, can be used to indicate proteins involved in the proliferation and differentiation of cells. In specific embodiments, polypeptides of the invention comprise the following amino acid sequence:

KVIDVIFSLPPGRKATFSCPLAPLSGAXGLPGGGANRPGPFLPCIQPWGPLRLP EGC (SEQ ID NO:471), MSSSLCPQGGKPPSLAPWPLCQGPXVCRVGVPT

GLALSSPASSHGGLCDCRKVAWLVPGPAQARG RAAWFYFYLTLFSVL (SEQ ID NO:472), and/or LALSSPASSHGGLCDCRKVAWLVPGP (SEQ ID NO:473). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in T cells, fetal liver, and to a lesser extent, in various normal and transformed tissues.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune, hematopoietic, or developmental disorders, including immunodeficiencies and cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.immune, hematopoietic, developmental, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:265 as residues: Arg-5 to Pro-12.

The tissue distribution in B-cells and fetal liver indicates that polynucleotides and polypeptides corresponding to this gene are useful for study and treatment of immune and developmental disorders. Moreover, polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of hematopoetic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. In addition, expression within fetal tissue and other cellular sources marked by proliferating cells indicates that this protein may play a role in the regulation of cellular division, and may show utility in the diagnosis and treatment of cancer and other proliferative disorders. Similarly, developmental tissues

rely on decisions involving cell differentiation and/or apoptosis in pattern formation. Thus this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:116 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 746 of SEQ ID NO:116, b is an integer of 15 to 760, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:116, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 107

One embodiment of this gene comprises the following amino acid sequence: MQRERWARPWMASTVESRMPEGKWRRFSTDLATWGATPARSWTKASRGSTT AWTRLPMRSTMVLDKQERKQRSLAMGSTTLLDRPGRKQTKRSKGSTLGSTRL GRKQRNLAKGSTMLLTRLERXWRSLAQVPTMLLARPGRSCRMLIMGSTKPAR RPTSC (SEQ ID NO:474). An additional embodiment is the polynucleotides encoding these polypeptides.

This gene is expressed primarily in keratinocytes and tissues undergoing wound healing, and to a lesser extent, in osteoblasts and smooth muscle.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, skin disorders; fibrosis; scarring; osteoporosis; osteopetrosis. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the skin, bone, or connective tissues, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. skin, bone, connective tissues, cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine,

synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:266 as residues: Gly-76 to Leu-83, Ala-108 to Glu-113, Ala-126 to Lys-132, Gly-145 to Leu-151.

The tissue distribution in keratinocytes indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and/or treatment of a variety of skin disorders. Elevated expression of this protein in skin and keratinocytes suggest that it may be involved in keratinocyte proliferation, survival, and/or differentiation. Thus, it may play a role in such processes as fibrosis and wound healing. Similarly, expression of this protein in osteoblasts indicates that it may also play a role in osteoblast survival, proliferation, and/or differentiation, and that it may be useful in the treatment of such disorders as osteoporosis or osteopetrosis.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:117 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 974 of SEQ ID NO:117, b is an integer of 15 to 988, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:117, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 108

The translation sequence of this gene shares homology with a mouse camodulin binding protein. The calcium-binding regulatory protein calmodulin is an essential subunit of the erythrocyte and other plasma membrane calcium ATPases. A rise in cytosolic calcium induces the binding of calcium ions to calmodulin, which triggers an allosteric activation of the calcium ATPase, and subsequently an export of calcium ions from the cell is accelerated.

This gene is expressed primarily in teratocarcinoma cells, and to a lesser extent, in myeloid progenitor cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, developmental defects, calcium-transport defects, in addition to immune or hematopoietic disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of embryonic and fetal tissues, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. developing tissues, immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:267 as residues: Tyr-124 to Gly-129.

The tissue distribution in teratocarcinoma cells indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of developmental defects as well as for organ regeneration. Moreover, expression within cellular sources marked by proliferating cells indicates that this protein may play a role in the regulation of cellular division, and may show utility in the diagnosis and treatment of cancer and other proliferative disorders. Similarly, developmental tissues rely on decisions involving cell differentiation and/or apoptosis in pattern formation. Thus this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Alternatively, the homology of the translation product of this gene to a mouse calmodulin binding protein indicates that the translation product of this gene may be useful for disorders involving calcium transport across the plasma membrane, for example. It has further been suggested this type of disorder may be responsible for disorders such as hypertension.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:118 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more

polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1933 of SEQ ID NO:118, b is an integer of 15 to 1947, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:118, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 109

One embodiment of this gene comprises polypeptides of the following amino acid sequence:
MRPLLGLLLVFAGCTFALYLLSTRLPRGRRLGSTEEAGGRSLWFPSDLAELREL SEVLREYRKEHQAYVFLLFCGAYLYKQGFAIPGSSFLNVLAGALFGPWLGLLL CCVLTSVGATCCYLLSSIFGKQLVVSYFPDKVALLQRKVEENRNSLFFFLLFLR LFPMTPNWFLNLSAPILNIPIVQFFFSVLIGLI PYNFICVQTGSILSTLTSLDA LFSWDTVFKLLAIAMVALIPGTLIKKFSQKHLQLNETSTANHIHSRKDT (SEQ ID NO:475). An additional embodiment is the polynucleotides encoding these polypeptides.

This gene is expressed primarily in ovarian tumor, and to a lesser extent, in smooth muscle and breast cancer.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, cancers, particularly of the ovary, musculature, and breast, such as rhabdomyosarcomas or fibroids. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproductive system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. ovaries, breast, cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, breast milk, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:268 as residues: Arg-24 to Arg-29.

The tissue distribution in ovarian tumor tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of

cancer, particularly ovarian and breast cancers. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:119 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1434 of SEQ ID NO:119, b is an integer of 15 to 1448, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:119, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 110

The translation product of this gene shares sequence homology with bovine acrosin inhibitors IIa and IIb which is thought to be important as protease inhibitors.

This gene is expressed primarily in keratinocytes.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, integumentary disorders, such as psoriasis, and wound healing abberations. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the integumental system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.integumentary, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:269 as residues: Tyr-39 to Lys-58.

The tissue distribution in keratinocytes, combined with the homology to the bovine acrosin inhibitors IIa and IIb indicates that polynucleotides and polypeptides

corresponding to this gene are useful for the acceleration of wound healing. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:120 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 482 of SEQ ID NO:120, b is an integer of 15 to 496, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:120, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 111

This gene is expressed primarily in fetal liver/spleen, T cells, and to a lesser extent, in bone marrow and primary dendritic cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, hematopoietic disorders; immune dysfunction; lymphomas. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:270 as residues: Glu-28 to His-34.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and/or treatment of hematopoietic disorders. This gene product is primarily expressed in hematopoietic cells

and tissues, suggesting that it plays a role in the survival, proliferation, and/or differentiation of hematopoieitic lineages. This is particularly supported by the expression of this gene product in fetal liver and bone marrow, the two primary sites of definitive hematopoiesis. Expression of this gene product in T cells and primary dendritic cells also strongly indicates a role for this protein in immune function and immune surveillance. Furthermore, since the gene is expressed in cells of lymphoid origin, the gene or protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:121 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1160 of SEQ ID NO:121, b is an integer of 15 to 1174, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:121, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 112

The gene encoding the disclosed cDNA is thought to reside on chromosome 14. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 14.

This gene is expressed primarily in fetal liver, spleen, and to a lesser extent in melanocyte.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to. developmental, integumentary, or hematopoeitic disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of fetal and embryonic tissues, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, developmental, integumentary, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine,

synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:271 as residues: Met-1 to Met-7, Gln-43 to Glu-50, Thr-89 to Thr-95.

The tissue distribution in fetal liver and spleen indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatment and diagnosis of developmental hematopoeitic disorders. Additionally, the tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and/or treatment of hematopoietic disorders. This gene product is primarily expressed in hematopoietic cells and tissues, suggesting that it plays a role in the survival, proliferation, and/or differentiation of hematopoieitic lineages. This is particularly supported by the expression of this gene product in fetal liver, which is a primary sites of definitive hematopoiesis, and strongly suggesting a role for this protein in immune function and immune surveillance.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:122 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1032 of SEQ ID NO:122, b is an integer of 15 to 1046, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:122, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 113

When tested against Jurkat T-cell lines, supernatants removed from cells containing this gene activated the GAS assay. Thus, it is likely that this gene activates T-cells through the Jak-STAT signal transduction pathway. The gamma activating sequence (GAS) is a promoter element found upstream of many genes which are involved in the Jak-STAT pathway. The Jak-STAT pathway is a large, signal transduction pathway involved in the differentiation and proliferation of cells. Therefore, activation of the Jak-STAT pathway, reflected by the binding of the GAS

element, can be used to indicate proteins involved in the proliferation and differentiation of cells.

This gene is expressed primarily in B cell lymphoma.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, B cell lymphoma. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:272 as residues: Gln-23 to Asn-31, Tyr-42 to Ser-58.

The tissue distribution in B-cells indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatment and diagnosis of lymphomas, particularly B cell lymphomas. Furthermore, expression of this gene product in B-cells indicates a role in the regulation of the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the gene or protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Additionally, the biological activity data supports the notion that the

translational product of this gene activates specific immune cells, and therefore may play a role in the initiation of immune system activity.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:123 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1146 of SEQ ID NO:123, b is an integer of 15 to 1160, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:123, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 114

This gene is expressed primarily in neutrophils: IL-1 and LPS induced.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in neutrophils indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of certain immune disorders, especially those involving neutrophils. Expression of this gene product in neutrophils indicates a role in the regulation of the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a

usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the gene or protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:124 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 879 of SEQ ID NO:124, b is an integer of 15 to 893, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:124, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 115

One embodiment of this gene comprises polpeptides of the following amino acid sequence: DIMPASVIFLICEGVLYGVQG (SEQ ID NO:476). An additional embodiment is the polynucleotides encoding these polypeptides.

This gene is expressed primarily in placenta.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, placental insufficiency; developmental abnormalities; aberrant angiogenesis; abnormal development and/or maintenance of the placenta. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the placenta and, more

generally, the vasculature and/or endothelium, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. developing, placental, cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in placental tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and/or treatment of disorders of the placenta. Specific expression within the placenta indicates that this gene product may play a role in the proper establishment and maintenance of placental function. Alternately, this gene product may be produced by the placenta and then transported to the embryo, where it may play a crucial role in the development and/or survival of the developing embryo or fetus. Expression of this gene product in a vascular-rich tissue such as the placenta also indicates that this gene product may be produced more generally in endothelial cells or within the circulation. In such instances, it may play more generalized roles in vascular function, such as in angiogenesis. It may also be produced in the vasculature and have effects on other cells within the circulation, such as hematopoietic cells. It may serve to promote the proliferation, survival, activation, and/or differentiation of hematopoietic cells, as well as other cells throughout the body.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:125 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1035 of SEQ ID NO:125, b is an integer of 15 to 1049, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:125, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 116

This gene is expressed primarily in keratinocytes, as well as in synovial hypoxia and T-cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, integumentary, immune, or skeletal disorders, particularly wound healing and rheumatoid conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the integumentary system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. skin, connective tissues, cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:275 as residues: Thr-42 to Pro-53, Val-78 to Glu-86, Glu-103 to Met-112, Ala-124 to Gly-131.

The tissue distribution in keratinocytes indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment of integumentary disorders, particularly with regard to wound healing. Furthermore, the tissue distribution also indicates that the translation product of this gene is useful for the treatment and/or detection of disorders of the connective tissues (e.g. arthritis, trauma, tendonitis, chrondomalacia and inflammation), such as in the diagnosis or treatment of various autoimmune disorders such as rheumatoid arthritis, lupus, scleroderma, and dermatomyositis as well as dwarfism, spinal deformation, and specific joint abnormalities as well as chondrodysplasias (ie. spondyloepiphyseal dysplasia congenita, familial osteoarthritis, Atelosteogenesis type II, metaphyseal chondrodysplasia type Schmid). Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:126 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of

a-b, where a is any integer between 1 to 1612 of SEQ ID NO:126, b is an integer of 15 to 1626, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:126, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 117

This gene is expressed primarily in hepatoma and testes tumor, and to a lesser extent, in brain.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, hepatic, neural, or reproductive disorders, particularly metastatic liver cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the cancer and metabolic systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. liver, brain, reproductive, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, seminal fluid, amniotic fluid, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in hepatic tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of some types of cancer including hepatoma, testes tumor and related metastases. Furthermore, the tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for the detection and treatment of liver disorders and cancers (e.g. hepatoblastoma, jaundice, hepatitis, liver metabolic diseases and conditions that are attributable to the differentiation of hepatocyte progenitor cells). Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:127 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome.

Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1163 of SEQ ID NO:127, b is an integer of 15 to 1177, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:127, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 118

This gene is expressed primarily in CD34 positive cells, and to a lesser extent, in pancreatic tumor and spleen.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, reproductive, endocrine, or immune disorders, particularly pancreatic cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the tumor, immune and metabolic systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, liver, spleen, cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, bile, amniotic fluid, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in pancreatic and CD34 positive cells indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of some types of cancer, especially those involving CD34 cells and pancreatic cancer. Furthermore, expression of this gene product in both CD34 positive cells and spleen indicates a role in the regulation of the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the gene or protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Therefore it may be also used as an agent for

immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, z, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:128 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1262 of SEQ ID NO:128, b is an integer of 15 to 1276, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:128, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 119

This gene is expressed primarily in osteoclastoma, fetal liver/spleen, and to a lesser extent, in primary dendritic cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, osteoclastoma; hematopoietic disorders; lymphomas; impaired immunity; immune disorders; inflammation, in addition to integumentary disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system and bone, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, bone, integumentary, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, amniotic fluid, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the

expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:278 as residues: Thr-23 to Pro-29, Thr-68 to Pro-76.

The tissue distribution in dendritic cells indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and/or treatment of bone and hematopoietic disorders. Elevated levels of expression of this gene product in osteoclastoma indicates that it may play a role in the survival, proliferation, and/or growth of osteoclasts. Therefore, it may be useful in influencing bone mass in such conditions as osteoporosis. More generally, as evidenced by expression in fetal liver/spleen, this gene may play a role in the survival, proliferation, and/or differentiation of hematopoietic cells in general, and may be of use in augmentation of the numbers of stem cells and committed progenitors. Expression of this gene product in primary dendritic cells also indicates that it may play a role in mediating responses to infection and controlling immunological responses, such as those that occur during immune surveillance.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:129 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1320 of SEQ ID NO:129, b is an integer of 15 to 1334, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:129, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 120

When tested against fibroblast cell lines, supernatants removed from cells containing this gene activated the EGR1 assay. Thus, it is likely that this gene activates fibroblast cells through a signal transduction pathway. Early growth response 1 (EGR1) is a promoter associated with certain genes that induces various tissues and cell types upon activation, leading the cells to undergo differentiation and proliferation.

This gene is expressed primarily in hemangiopericytoma.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, soft tissue cancers, such as hemangiopericytoma, in addition to other proliferative conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the vascular system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. circulatory system, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:279 as residues: Pro-49 to Thr-64.

The tissue distribution indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of hemangiopericytoma. Furthermore, the biological activity data demonstrates that the translation product of this gene activates fibroblast cells. Fibroblast cells have the abiliy to undergo vascularization, and thus the translation product of this gene may be involved in disorders of the vascular tissue, such as hemangiopericytoma.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:130 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 518 of SEQ ID NO:130, b is an integer of 15 to 532, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:130, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 121

This gene is expressed primarily in kidney cortex.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, renal or urogenital disorders, particularly nephritis. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the renal system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. kidney, cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:280 as residues: Pro-33 to Ser-38.

The tissue distribution in kidney cortex indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of diseases of the kidney, including nephritis. Furthermore, the tissue distribution in kidney indicates that this gene or gene product could be used in the treatment and/or detection of kidney diseases including renal failure, renal tubular acidosis, proteinuria, pyuria, edema, pyelonephritis, hydronephritis, nephrotic syndrome, crush syndrome, glomerulonephritis, hematuria, renal colic and kidney stones, in addition to Wilms Tumor Disease, and congenital kidney abnormalities such as horseshoe kidney, polycystic kidney, and Falconi's syndrome. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:131 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 671 of SEQ ID NO:131, b is an integer of 15 to 685, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:131, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 122

This gene is expressed primarily in spleen from chronic lymphocytic leukemia.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune or hematopoietic disordes, such as chronic lymphocytic leukemia. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. spleen, cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in spleen tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of chronic lymphocytic leukemia. Furthermore, the expression observed predominantly in spleen cells also indicates that the polynucleotides or polypeptides are important in treating and/or detecting hematopoietic disorders, such as graft versus host reaction, graft versus host disease, transplant rejection, myelogenous leukemia, bone marrow fibrosis, and myeloproliferative disease. The polypeptides or polynucleotides are also useful to enhance or protect proliferation, differentiation, and functional activation of hematopoietic progenitor cells (e.g., bone marrow cells), useful in treating cancer patients undergoing chemotherapy or patients undergoing bone marrow transplantation. The polypeptides or polynucleotides are also useful to increase the proliferation of peripheral blood leukocytes, which can be used in the combat of a range of hematopoietic disorders, including immmunodeficiency diseases, leukemia, and septicemia.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:132 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome.

Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 715 of SEQ ID NO:132, b is an integer of 15 to 729, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:132, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 123

This gene is expressed primarily in neutrophils, dendritic cells, and CD34 positive cells (Cord Blood).

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune, hematopoietic, or developmental disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, developmental, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, amniotic fluid, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in neutrophils indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of some types of immune disorders, especially those involving neutrophils. More generally, as evidenced by expression in CD34 positive cells, this gene may play a role in the survival, proliferation, and/or differentiation of hematopoietic cells in general, and may be of use in augmentation of the numbers of stem cells and committed progenitors. Expression of this gene product in primary dendritic cells also indicates that it may play a role in mediating responses to infection and controlling immunological responses, such as those that occur during immune surveillance.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:133 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the

scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1065 of SEQ ID NO:133, b is an integer of 15 to 1079, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:133, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 124

This gene is expressed primarily in adult lung.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, respiratory disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the respiratory system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. respiratory, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in lung tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatment and diagnosis of respiratory disorders, such as asthma, emphysema, and ARDS. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:134 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1283 of SEQ ID NO:134, b is an integer of 15

to 1297, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:134, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 125

The gene encoding the disclosed cDNA is thought to reside on chromosome 19. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 19.

This gene is expressed primarily in T-cell lymphoma and fetal liver/spleen.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune, developmental, or hematopoietic disorders, particularly lymphomas. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, developmental, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, amniotic fluid, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:284 as residues: Gln-25 to Phe-43.

The tissue distribution in T-cells indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of T-cell lymphoma. Furthermore, expression of this gene product in fetal liver/spleen indicates a role in the regulation of the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the gene or protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma,

immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:135 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 603 of SEQ ID NO:135, b is an integer of 15 to 617, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:135, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 126

The translation product of this gene shares sequence homology with C9, a gene of unknown function. The gene encoding the disclosed cDNA is thought to reside on chromosome 3. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 3. One embodiment of this gene comprises the polypeptides of the following amino acid sequence:
GTAFQHAFSTNDCSRNVYIKKNGFTLHRNPIAQSTDGARTKIGFSEGRHAWEV
WWEGPLGTVAVIGIATKRAPMQCQGYVALLGSDDQSWGWNLVDNNLLHNGE
VNGSFPQCNNAPKYQIGERIRVILDMEDKTLAFERGYEFLGVAFRGLPKVCLYP
AVSAVYGNTEVTLVYLGKPLDG (SEQ ID NO:477). An additional embodiment is the polynucleotides encoding these polypeptides.

This gene is expressed primarily in placenta, and to a lesser extent, in apoptotic T-cells, as well as in smooth muscle, testes, and microvascular endothelial cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune or reproductive disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes

for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, reproductive, muscular, vascular, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, amniotic fluid, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in T-cells combined with the homology to the C9 protein indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of some immune disorders, especially those involving T-cells. Furthermore, this gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses), or male infertility. Since the gene is expressed in cells of lymphoid origin, the gene or protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:136 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1297 of SEQ ID NO:136, b is an integer of 15 to 1311, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:136, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 127

This gene is expressed primarily in neutrophils.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune or hematopoietic disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes

for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in neutrophils indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of some immune disorders, especially those involving neutrophils. Furthermore, as evidenced by expression in neutrophils, this gene may play a role in the survival, proliferation, and/or differentiation of hematopoietic cells in general, and may be of use in augmentation of the number of stem cells and committed progenitors. Expression of this gene product in neutrophils further indicates that it may play a role in mediating responses to infection and controlling immunological responses, such as those that occur during immune surveillance. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:137 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1081 of SEQ ID NO:137, b is an integer of 15 to 1095, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:137, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 128

This gene is expressed primarily in neutrophils; IL-1 and LPS induced.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are

not limited to, immune or hematopoietic disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:287 as residues: Lys-36 to Asp-42.

The tissue distribution in neutrophils indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of some immune disorders, especially those involving neutrophils. Furthermore, as evidenced by the expression in neutrophils, this gene may play a role in the survival, proliferation, and/or differentiation of hematopoietic cells in general, and may be of use in augmentation of the number of stem cells and committed progenitors. Expression of this gene product in neutrophils further indicates that it may play a role in mediating responses to infection and controlling immunological responses, such as those that occur during immune surveillance. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:138 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 678 of SEQ ID NO:138, b is an integer of 15 to 692, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:138, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 129

This gene is expressed primarily in neutrophils, IL-1 and LPS induced.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune or hematopoietic disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:288 as residues: Pro-32 to Gln-38, Gly-51 to Asp-57.

The tissue distribution in neutrophils indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of certain immune disorders, especially those involving neutrophils. Furthermore, as evidenced by expression in neutrophils, this gene may play a role in the survival, proliferation, and/or differentiation of hematopoietic cells in general, and may be of use in augmentation of the number of stem cells and committed progenitors. Expression of this gene product in nuetrophils further indicates that it may play a role in mediating responses to infection and controlling immunological responses, such as those that occur during immune surveillance. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:139 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 734 of SEQ ID NO:139, b is an integer of 15

to 748, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:139, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 130

This gene is expressed primarily in neutrophils, IL-1 and LPS induced.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. immune, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:289 as residues: Gly-22 to Ser-28.

The tissue distribution in neutrophils indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of certain immune disorders involving neutrophils. Furthermore, as evidenced by expression in neutrophils, this gene may play a role in the survival, proliferation, and/or differentiation of hematopoietic cells in general, and may be of use in augmentation of the number of stem cells and committed progenitors. Expression of this gene product in neutrophils further indicates that it may play a role in mediating responses to infection and controlling immunological responses, such as those that occur during immune surveillance. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:140 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome.

Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1118 of SEQ ID NO:140, b is an integer of 15 to 1132, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:140, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 131

This gene is expressed primarily in corpus callosum.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neural disorders, particularly diseases of the brain, such as neurodegenerative disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. brain, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in neural tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of brian disorders and diseases, including paranoia, schizophrenia, depression, mania, and Alzheimer's disease. Furthermore, elevated expression of this gene product within the corpus callosum of the brain indicates that it may be involved in neuronal survival; synapse formation; conductance; neural differentiation, etc. Such involvement may impact many processes, such as learning and cognition. Again, it may also be useful in the treatment of such neurodegenerative disorders as schizophrenia; ALS; or Alzheimer's. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:141 and may have been publicly available prior to conception of the present

invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1098 of SEQ ID NO:141, b is an integer of 15 to 1112, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:141, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 132

The translation product of this gene shares sequence homology with the putative transposase of the Tigger-1 transposon.

This gene is expressed primarily in atrophic endometrium.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, muscular disorders, particularly muscular atrophy. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproductive system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g. reproductive, muscular, endocrine, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in endometrial tissue combine with the homology to a transposase indicates that polynucleotides and polypeptides corresponding to this gene are useful for DNA repair in atrophying tissue, particularly of the endometrium. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:142 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome.

Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1070 of SEQ ID NO:142, b is an integer of 15 to 1084, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:142, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 133

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: ARAFQHLMVADHSHFHRTLIKQPSMIPNATFYHIF (SEQ ID NO:478). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in hemangiopericytoma.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, soft tissue tumors, particularly hemangiopericytoma, or other proliferative disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the vascular system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.immune, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:292 as residues: Ser-39 to Ser-44.

The tissue distribution in hemangiopericytoma indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of various soft-tissue tumors, in addition to other proliferative disorders which may afflict other tissues or cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ

ID NO:143 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1036 of SEQ ID NO:143, b is an integer of 15 to 1050, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:143, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 134

This gene is expressed primarily in hypothalamus of a schizophrenic patient, and to a lesser extent in spleen.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neural or immune disorders,particularly Schizophrenia or neurodegenerative conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous and immune systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.neural, immune, hematopoietic, spleen, cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in hypothalamus indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of Schizophrenia, as well as other central nervous system and immune system disorders. Furthermore, polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states, behavioural disorders, or inflamatory conditions such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, meningitis, encephalitis, demyelinating diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, schizophrenia, mania,

dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses , autism, and altered bahaviors, including disorders in feeding, sleep patterns, balance, and preception. In addition, elevated expression of this gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or survival.Moreover, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, disorders of the endocrine system, or disorders of the cardiovascular system. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:144 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1099 of SEQ ID NO:144, b is an integer of 15 to 1113, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:144, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 135

The translation product of this gene shares sequence homology with a chicken ring-finger-zinc finger protein, C-RZF, in addition to, the human multiple membrane spanning receptor TRC8 which is thought to serve as a signaling receptor in renal and thyroid carcinomas. (See Genbank Accession No.gil3395787 (AF064801)) The TRC8 locus has been described in a family with classical features of hereditary renal cell carcinoma. The 8q24.1 (locus of TRC8) breakpoint region encodes the 664-aa multiple membrane spanning protein, TRC8, with similarity to the hereditary basal cell carcinoma/segment polarity gene, patched. This similarity involves two regions of patched, the putative sterol-sensing domain and the second extracellular loop that participates in the binding of sonic hedgehog. In the 3;8 translocation, TRC8 is fused to FHIT (fragile histidine triad gene) and is disrupted within the sterol-sensing domain. In

contrast, the FHIT coding region is maintained and expressed. In a series of sporadic renal carcinomas, an acquired TRC8 mutation was identified. In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: ARALPEIKGSRLQEINDVCAICYHEFTTSARITPCNHYFHALCLRKWLYIQDTCP MCHQKVYIEDDIKDN SNVSNNNGFIPPNETPEEAVREAAAESDRELNEDDSTDCDDDVQRERNGVIQHT GAAAGRI (SEQ ID NO:479), FSTQAQQLEEFNDDTD (SEQ ID NO:480), RLQE INDVCAICYHEFTTSARI (SEQ ID NO:481), LYIQDTCPMCHQKVYIEDDI (SEQ ID NO:482), VSNNNGFIPPNETPEEAVREA (SEQ ID NO:483), and/or DDSTDCD DDVQRERNGVIQHTGAAAG (SEQ ID NO:484). Polynucleotides encoding these polypeptides are also encompassed by the invention. The gene encoding the disclosed cDNA is believed to reside on chromosome 8. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 8.

This gene is expressed primarily in human embryonic tissues.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, developmental abnormalities, particularly congenital defects or proliferative conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the embryonic tissues, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.developmental, renal, endocrine, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in embryonic tissue, combined with the homology to ring finger-zinc finger protein and the human TRC8 receptor indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of abnormalities of the embryonic tissues, in particular proliferative disorders. In addition, polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis, detection, and/or treatment of developmental disorders. The relatively specific expression of this gene product during embryogenesis indicates that it may be a key player in the proliferation, maintenance, and/or differentiation of various cell types during development. It may also act as a morphogen to control cell and tissue type

specification. Because of potential roles in proliferation and differentiation, this gene product may have applications in the adult for tissue regeneration and the treatment of cancers. Moreover,this protein may show utility in the diagnosis and treatment of cancer and other proliferative disorders. Similarly, developmental tissues rely on decisions involving cell differentiation and/or apoptosis in pattern formation. Thus this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:145 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 671 of SEQ ID NO:145, b is an integer of 15 to 685, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:145, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 136

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: VAGITGAHHHAQLIFVLLVEMGFHHV GQAGLKLLTSDN PRTSASQSAGITGMSXGRRITCGQEFKTAVSYNCTTALQPDRAKLCFLFKKKK KISIQ RTLPGIKRVIYNYERVDSSKGHNSQVQWAHA CNPSTLGGRGGQIV (SEQ ID NO:485), AGITGAHHHAQLIFVLLVEMGF (SEQ ID NO:486), RVIYN YERVDSSKGHNSQVQWAHACNP (SEQ ID NO:487). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in microvascular endothelial cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, vascular or endothelial disorders, such as the following: arteriosclerosis, tumorigenesis, stroke, embolism, aneurysm, microvascular disease, and various cardiovascular disorders. Similarly, polypeptides and antibodies directed to these

polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the vascular system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.vascular, endothelial, cardiovascular, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in microvascular endothelial tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of vascular disorders. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:146 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1024 of SEQ ID NO:146, b is an integer of 15 to 1038, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:146, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 137

The gene encoding the disclosed cDNA is believed to reside on chromosome 2. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 2.

This gene is expressed primarily in fetal tissues, most notably fetal cochlea and fetal lung, and to a lesser extent, in rhabdomyosarcoma and healing groin wound tissue.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are

not limited to, embryological/developmental abnormalities; hearing defects; respiratory diseases; rhabdomyosarcoma; general cancers and other proliferative conditions; fibrosis; wound healing. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the embryo/fetus or of striated muscle cells, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.developmental, pulmonary, auditory, muscle, fibroid, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in fetal tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for diseases involving abnormal cellular proliferation, such as cancer. Expression of this gene product in rapidly proliferating cells, such as those found in the embryo; in rhabdomyosarcomas; and in wound healing tissue, indicates that this gene may play a role in controlling or promoting cell proliferation. Alternately, expression of this gene in fetal tissues indicates that it may play a role in cellular development and differentiation, particularly of the auditory system as well as the lungs. Thus, this gene product may be useful in the treatment and/or diagnosis of hearing defects, as well as respiratory disorders. Expression of this gene product in rhabdomyosarcoma indicates that it may play a role in the progression of such cancers, and may also be involved in metastasis and/or angiogenesis. Additionally, expression in wound healing tissues again indicates a role in the proliferation of connective tissue types involved in wound healing, as well as in the fibrosis and scarring that accompanies the wound healing process. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:147 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 837 of SEQ ID NO:147, b is an integer of 15

to 851, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:147, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 138

The gene encoding the disclosed cDNA is believed to reside on chromosome 1. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 1.

This gene is expressed primarily in adult brain, and to a lesser extent, in cerebellum.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, disorders and diseases of the brain, particularly neurodegenerative and behavior conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.neural, cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:297 as residues: Pro-25 to Ser-30, Thr-36 to Ser-47.

The tissue distribution in neural tissues indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatment and diagnosis of disorders and diseases of the brain, particularly paranoia, Alzheimer's, depression, schizophrenia, and mania. Moreover, polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states, behavioural disorders, or inflamatory conditions such as Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, meningitis, encephalitis, demyelinating diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses , autism, and altered bahaviors, including disorders in feeding, sleep patterns, balance,

and preception. In addition, elevated expression of this gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or survival.Moreover, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:148 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 600 of SEQ ID NO:148, b is an integer of 15 to 614, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:148, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 139

This gene is expressed primarily in cerebellum.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to. neural disorders, particularly neurodegenerative disorders, such as Alzheimers. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.neural, cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in cerebellum indicates that polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of brain diseases and disorders. Specifically, polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states, behavioural disorders, or inflamatory conditions such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, meningitis, encephalitis, demyelinating diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses , autism, and altered bahaviors, including disorders in feeding, sleep patterns, balance, and preception. In addition, elevated expression of this gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or survival.Moreover, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:149 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1186 of SEQ ID NO:149, b is an integer of 15 to 1200, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:149, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 140

This gene is expressed primarily in brain tissue of a patient with Alzheimer's disease, and to a lesser extent, in human adipose tissue.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a

biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neural or adipose-related disorders, particularly neurodegenerative disorders, such as Alzheimer's disease. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.neural, metabolic, adipose, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in neural and adipose tissues indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of Alzheimer's disease and other nervous system disorders. Moreover, polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states, behavioural disorders, or inflamatory conditions such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, meningitis, encephalitis, demyelinating diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses , autism, and altered bahaviors, including disorders in feeding, sleep patterns, balance, and preception. In addition, elevated expression of this gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or survival.Moreover, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. More specifically, the protein product of this gene may show utility in the treatment, diagnosis, and/or prevention of neural disorders which occur secondary to aberrations in fatty-acid metabolism, such as improper development of the myelin sheath of nerve cells, for example. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ

ID NO:150 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 669 of SEQ ID NO:150, b is an integer of 15 to 683, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:150, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 141

This gene is expressed primarily in T cells.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune or hematopoietic disorders, particularly T cell leukemia, immunodeficiencies, and inflammatory conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:300 as residues: Asn-62 to Leu-68.

The tissue distribution T-cells indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of T cell leukemia and other disorders of the immune system. Moreover, this gene product may play a role in regulating the proliferation; survival; differentiation; and/or activation of hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene

product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immunodeficiency diseases such as AIDS, leukemia, rheumatoid arthritis, granulomatous disease, inflammatory bowel disease, sepsis, acne, neutropenia, neutrophilia, psoriasis, hypersensitivities, such as T-cell mediated cytotoxicity; immune reactions to transplanted organs and tissues, such as host-versus-graft and graft-versus-host diseases, or autoimmunity disorders, such as autoimmune infertility, lense tissue injury, demyelination, systemic lupus erythematosis, drug induced hemolytic anemia, rheumatoid arthritis, Sjogren's disease, scleroderma and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:151 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 813 of SEQ ID NO:151, b is an integer of 15 to 827, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:151, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 142

The gene encoding the disclosed cDNA is believed to reside on chromosome 8. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 8.

This gene is expressed primarily in the frontal lobe of the brain, and to a lesser extent, in synovial fluid and embryos.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, developmental or neural disorders, particularly neurodegenerative, behavioral, and congenital abnormalities of the brain. Similarly, polypeptides and

antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.neural, developmental, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:301 as residues: Gln-24 to Lys-31.

The tissue distribution in brain tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and treatment of abnormalities of the brain. Moreover, polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states, behavioural disorders, or inflamatory conditions such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, meningitis, encephalitis, demyelinating diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses , autism, and altered bahaviors, including disorders in feeding, sleep patterns, balance, and preception. In addition, elevated expression of this gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or survival.Moreover, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the skeletal or cardiovascular system. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:152 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more

polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 821 of SEQ ID NO:152, b is an integer of 15 to 835, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:152, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 143

The gene encoding the disclosed cDNA is believed to reside on chromosome 19. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 19.

This gene is expressed primarily in osteoblasts.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, skeletal disorders, such as osteoporosis, and cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the skeletal system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.skeletal, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in osteoblasts indicates that polynucleotides and polypeptides corresponding to this gene are useful for treatment of osteoporosis and other bone degenerative diseases.Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:153 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of

a-b, where a is any integer between 1 to 544 of SEQ ID NO:153, b is an integer of 15 to 558, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:153, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 144

This gene is expressed primarily in CD34 positive cells (cord blood) and placenta.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, developmental and immune disorders, particularly proliferative conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.immune, reproductive, developmental, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in cord blood and placental tissues indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of certain immune disorders, especially those involving CD34 cells. Expression within cellular sources marked by proliferating cells indicates that this protein may play a role in the regulation of cellular division, and may show utility in the diagnosis and treatment of cancer and other proliferative disorders. Similarly, developmental tissues rely on decisions involving cell differentiation and/or apoptosis in pattern formation. Thus this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:154 and may have been publicly available prior to conception of the present

invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1187 of SEQ ID NO:154, b is an integer of 15 to 1201, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:154, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 145

This gene is expressed primarily in frontal cortex of the brain.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neural or spinal cord disorders, such as neurodegenerative conditions and other abnormalities of the brain. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous system, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.neural, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:304 as residues: Pro-21 to Ser-27.

The tissue distribution in frontal cortex tissue indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of the abnormalities of the brain. Specfically, polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states, behavioural disorders, or inflamatory conditions such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, meningitis, encephalitis, demyelinating diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, schizophrenia, mania, dementia, paranoia, obsessive compulsive

disorder, panic disorder, learning disabilities, ALS, psychoses , autism, and altered bahaviors, including disorders in feeding, sleep patterns, balance, and preception. In addition, elevated expression of this gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or survival.Moreover, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:155 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1012 of SEQ ID NO:155, b is an integer of 15 to 1026, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:155, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 146

The gene encoding the disclosed cDNA is believed to reside on chromosome 2. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 2.

This gene is expressed primarily in adrenal gland tumor, breast tissue, and to a lesser extent in adipose tissue.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, endocrine or reproductive disorders, such as adrenal gland tumor; breast cancer; metabolic disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the adrenal glands and breast, expression of this gene at significantly

higher or lower levels may be detected in certain tissues or cell types (e.g.reproductive, metabolic, endocrine, breast, adrenal gland, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, breast milk, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:305 as residues: Arg-44 to Lys-49, Asp-60 to Phe-66.

The tissue distribution in adrenal gland and breast tissues indicates that polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis and/or treatment of disorders involving the adrenal gland. Expression of this gene product in adrenal gland tumor indicates that it may play a role in the proliferation of cells of the adrenal gland, or potentially in the proliferation of cells in general. In such an event, it may play a role in determining the course and severity of cancer. Alternatively, it may play a role in the normal function of adrenal glands, such as in the production of corticosteroids, androgens, or epinephrines. Thus it may play a role in general homeostasis, as well as in disorders involving the androgen hormones. Expression of this gene product in breast and adipose tissues also indicates that it may play a role in breast cancer, or in supplying vital nutrients to the infant during lactation. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:156 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 890 of SEQ ID NO:156, b is an integer of 15 to 904, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:156, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 147

This gene is expressed primarily in LNCAP, and untreated spleen; metastic melanoma.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune, hematopoietic, integumentary disorders, such as metastic melanoma. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and cancer metabolic systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.immune, hematopoietic, integumentary, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Preferred epitopes include those comprising a sequence shown in SEQ ID NO:306 as residues: His-47 to Thr-53.

The tissue distribution in spleen and integumentary tissues indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of some types of cancer, especially metastic melanoma. The protein product of this gene is useful for the treatment, diagnosis, and/or prevention of various skin disorders including congenital disorders (i.e. nevi, moles, freckles, Mongolian spots, hemangiomas, port-wine syndrome), integumentary tumors (i.e. keratoses, Bowen's disease, basal cell carcinoma, squamous cell carcinoma, malignant melanoma, Paget's disease, mycosis fungoides, and Kaposi's sarcoma), injuries and inflammation of the skin (i.e.wounds, rashes, prickly heat disorder, psoriasis, dermatitis), atherosclerosis, uticaria, eczema, photosensitivity, autoimmune disorders (i.e. lupus erythematosus, vitiligo, dermatomyositis, morphea, scleroderma, pemphigoid, and pemphigus), keloids, striae, erythema, petechiae, purpura, and xanthelasma. In addition, such disorders may predispose increased susceptibility to viral and bacterial infections of the skin (i.e. cold sores, warts, chickenpox, molluscum contagiosum, herpes zoster, boils, cellulitis, erysipelas, impetigo, tinea, althletes foot, and ringworm). Moreover, the protein product of this gene may also be useful for the treatment or diagnosis of various connective tissue disorders such as arthritis, trauma, tendonitis, chrondomalacia and inflammation, autoimmune disorders such as rheumatoid arthritis, lupus, scleroderma, and dermatomyositis as well as dwarfism, spinal deformation, and specific joint abnormalities as well as chondrodysplasias (ie. spondyloepiphyseal dysplasia congenita, familial osteoarthritis, Atelosteogenesis type

II, metaphyseal chondrodysplasia type Schmid). Alternatively, this gene is useful for the treatment and diagnosis of hematopoetic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:157 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 902 of SEQ ID NO:157, b is an integer of 15 to 916, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:157, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 148

In specific embodiments, polypeptides of the invention comprise the following amino acid sequence: AGAEVVMLFLLTPSS HHQHECVRRAFECGDCHILLDNNV LGVDCHGAGERAVHLEDHFVHIDTISLLLEDALEYSALIAGHPKSD LPPGLSRC RPWEHHWPISYTG (SEQ ID NO:488), TI SYLCNNVSYMQLQKLVGKSMIFLP YSLPIHLPGNHRLLLPRVGMRLRGCCFSPYIITDFKWC (SEQ ID NO:489), EMGQWCSQGLHLDSPGGKSDFGCPAINAEYSRASSKSRLMVSMWTKWSSRC TALSPAP (SEQ ID NO:490), RAFECGDCHILLDNNVLGVDCHGAG (SEQ ID NO:491), and/or LVGKSMIFLPYSLPIHLPGNHRL (SEQ ID NO:492). Polynucleotides encoding these polypeptides are also encompassed by the invention. The gene encoding the disclosed cDNA is believed to reside on chromosome 1.

Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 1.

This gene is expressed primarily in ovary, and to a lesser extent in meninges, the adrenal gland, and the cerebellum.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, reproductive, neural, and endocrine disorders, such as ovarian and brain cancers, neurodeficiency disorders, and infertility. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the female reproductive and endocrine systems, expression of this gene at significantly higher or lower levels may be detected in certain tissues or cell types (e.g.neural, reproductive, ovarian, and cancerous and wounded tissues) or bodily fluids (e.g.lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in ovarian and endocrine tissues indicates that polynucleotides and polypeptides corresponding to this gene are useful for diagnosis and treatment of ovarian cancer and other endrocrine disorders. Alternatively, polynucleotides and polypeptides corresponding to this gene are useful for the detection/treatment of neurodegenerative disease states, behavioural disorders, or inflamatory conditions such as Alzheimers Disease, Parkinsons Disease, Huntingtons Disease, Tourette Syndrome, meningitis, encephalitis, demyelinating diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses , autism, and altered bahaviors, including disorders in feeding, sleep patterns, balance, and preception. In addition, elevated expression of this gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or survival.Moreover, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Protein, as well

as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:158 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 907 of SEQ ID NO:158, b is an integer of 15 to 921, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:158, and where b is greater than or equal to a + 14.

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
1	HNGEU17	209299 09/25/97	Uni-ZAP XR	11	826	1	826	277	277	160	1	17	18	23
2	HNGDJ72	209299 09/25/97	Uni-ZAP XR	12	524	1	524	185	185	161	1	19	20	113
3	HNGEO29	209299 09/25/97	Uni-ZAP XR	13	491	1	491	98	98	162	1	32	33	44
4	HNHDL95	209299 09/25/97	Uni-ZAP XR	14	403	1	403	121	121	163	1	23	24	58
5	HAGDS35	209299 09/25/97	Uni-ZAP XR	15	813	1	813	52	52	164	1	23	24	118
6	HNGEQ48	209299 09/25/97	Uni-ZAP XR	16	264	1	264	10	10	165	1	20	21	54
7	HNGDG40	209299 09/25/97	Uni-ZAP XR	17	520	1	520	13	13	166	1	36	37	127

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
8	HNGEN81	209299 09/25/97	Uni-ZAP XR	18	993	1	993	380	380	167	1	25	26	56
9	H2MAC30	209299 09/25/97	pBluescript SK-	19	459	1	459	157	157	168	1	28	29	72
10	hnhfb16	209299 09/25/97	Uni-ZAP XR	20	555	1	555	344	344	169	1	23	24	70
11	HPFCL43	209299 09/25/97	Uni-ZAP XR	21	665	1	665	21	21	170	1	17	18	79
12	HSATR82	209299 09/25/97	Uni-ZAP XR	22	777	1	777	74	74	171	1	15	16	41
13	H6EDF66	209299 09/25/97	Uni-ZAP XR	23	540	1	540	146	146	172	1	27	28	131
14	HNHIC21	209299 09/25/97	Uni-ZAP XR	24	484	1	484	65	65	173	1	16	17	44
15	HOVCA92	209299 09/25/97	pSport1	25	707	1	488	181	181	174	1	20	21	62

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
16	HNHDW38	209299 09/25/97	Uni-ZAP XR	26	793	1	793	66	66	175	1	19	20	19
17	HSDIL30	209299 09/25/97	Uni-ZAP XR	27	638	1	638	26	26	176	1	33	34	40
18	HATDB65	209299 09/25/97	Uni-ZAP XR	28	528	14	528	110	110	177	1	40	41	48
19	HPMSM14	209299 09/25/97	pBluescript	29	919	1	919	119	119	178	1	46	47	106
20	HTTEA24	209299 09/25/97	Uni-ZAP XR	30	864	1	864	133	133	179	1	20	21	45
21	HAGDS20	209299 09/25/97	Uni-ZAP XR	31	919	1	919	11	11	180	1	17	18	66
22	HSDJM30	209299 09/25/97	Uni-ZAP XR	32	956	1	956	70	70	181	1	24	25	49
23	HNHEE88	209299 09/25/97	Uni-ZAP XR	33	566	1	566	87	87	182	1	19	20	72

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
24	HSLFD55	209346 10/09/97	Uni-ZAP XR	34	1564	1	1564	105	105	183	1	21	22	43
25	HSAXJ29	209299 09/25/97	Uni-ZAP XR	35	1035	1	1035	129	129	184	1	19	20	57
26	HSFAM39	209299 09/25/97	Uni-ZAP XR	36	620	1	620	117	117	185	1	23	24	68
27	HTODO72	209299 09/25/97	Uni-ZAP XR	37	973	1	973	183	183	186	1	16	17	24
28	HADDZ85	209299 09/25/97	pSport1	38	838	1	838	270	270	187	1	36	37	57
29	HDPCM26	209300 09/25/97	pCMVSport 3.0	39	607	1	607	174	174	188	1	19	20	66
30	HSZAA13	209300 09/25/97	Uni-ZAP XR	40	882	1	855	147	147	189	1	19	20	88
31	HDTBP04	209300 09/25/97	pCMVSport 2.0	41	959	1	959	65	65	190	1	15	16	220

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
32	HHGCQ54	209300 09/25/97	Lambda ZAP II	42	875	1	875	62	62	191	1	15	16	51
33	HSNAB12	209300 09/25/97	Uni-ZAP XR	43	630	1	630	151	151	192	1	27	28	71
34	HBJID05	209300 09/25/97	Uni-ZAP XR	44	571	1	571	137	137	193	1	20	21	111
35	HSNBM49	209300 09/25/97	Uni-ZAP XR	45	930	1	930	27	27	194	1	21	22	60
36	HJMBF77	209300 09/25/97	pCMVSport 3.0	46	437	1	432	60	60	195	1	24	25	126
37	HJMBM38	209300 09/25/97	pCMVSport 3.0	47	1024	316	1023	387	387	196	1	15	16	112
38	HHGCL33	209300 09/25/97	Lambda ZAP II	48	463	1	463	74	74	197	1	20	21	65
39	HCEWE20	209300 09/25/97	Uni-ZAP XR	49	885	13	885	166	166	198	1	18	19	51

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
40	HCUHL13	209300 09/25/97	ZAP Express	50	847	1	847	84	84	199	1	20	21	58
41	HBJHO68	209300 09/25/97	Uni-ZAP XR	51	580	1	580	34	34	200	1	24	25	51
42	HCWDV84	209300 09/25/97	ZAP Express	52	598	1	598	47	47	201	1	25	26	80
43	HBXFC78	209300 09/25/97	ZAP Express	53	571	1	567	184	184	202	1	14	15	69
44	HE2FI45	209300 09/25/97	Uni-ZAP XR	54	1247	212	1082	273	273	203	1	38	39	45
45	HEOMG13	209300 09/25/97	pSport1	55	848	182	848	247	247	204	1	27	28	52
46	HFAMH77	209300 09/25/97	Uni-ZAP XR	56	669	96	669	240	240	205	1	33	34	61
47	HSVCF20	209300 09/25/97	Uni-ZAP XR	57	680	1	680	43	43	206	1	25	26	43

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
48	HISAG02	209300 09/25/97	pSport1	58	524	1	524	18	18	207	1	27	28	40
49	HCDAF84	209300 09/25/97	Uni-ZAP XR	59	427	1	427	168	168	208	1	18	19	56
50	HHAAC17	209300 09/25/97	Uni-ZAP XR	60	1263	1	1263	227	227	209	1	19	20	125
51	HSNMC45	209300 09/25/97	Uni-ZAP XR	61	720	1	720	232	232	210	1	19	20	25
52	HEQAG39	209300 09/25/97	pCMVSport 3.0	62	589	69	589	93	93	211	1	19	20	47
53	HKACH44	209300 09/25/97	pCMVSport 2.0	63	686	1	686	375	375	212	1	25	26	44
54	HBNBG49	209300 09/25/97	Uni-ZAP XR	64	452	1	452	40	40	213	1	34	35	51
55	HE2EN04	209300 09/25/97	Uni-ZAP XR	65	370	1	370	57	57	214	1	16	17	50

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
56	HSVAA10	209300 09/25/97	Uni-ZAP XR	66	987	1	987	38	38	215	1	16	17	209
57	HFPBA88	209300 09/25/97	Uni-ZAP XR	67	1018	284	1018	33	33	216	1	38	39	195
57	HFPBA88	209300 09/25/97	Uni-ZAP XR	159	804	70	804	98	98	308	1	41	42	102
58	HFTBM50	209300 09/25/97	Uni-ZAP XR	68	762	1	740	158	158	217	1	20	21	34
59	HHEBW54	209300 09/25/97	pCMVSport 3.0	69	630	1	630	97	97	218	1	37	38	71
60	HFEBH21	209300 09/25/97	Uni-ZAP XR	70	940	1	940	21	21	219	1	30	31	52
61	HFTDZ36	209300 09/25/97	Uni-ZAP XR	71	1103	231	1103	547	547	220	1	22	23	68
62	HGLAW96	209300 09/25/97	Uni-ZAP XR	72	899	246	899	308	308	221	1	24	25	68

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
63	HKAFK41	209300 09/25/97	pCMVSport 2.0	73	549	1	549	243	243	222	1	30	31	43
64	HOSEG51	209324 10/02/97	Uni-ZAP XR	74	590	48	590	232	232	223	1	31	32	102
65	HTEJT39	209324 10/02/97	Uni-ZAP XR	75	1056	1	1056	146	146	224	1	32	33	213
66	HPTRH45	209324 10/02/97	pBluescript	76	930	1	930	92	92	225	1	26	27	108
67	HDHMA72	209324 10/02/97	pCMVSport 2.0	77	4463	216	2158	287	287	226	1	36	37	315
68	HNTBL27	209324 10/02/97	pCMVSport 3.0	78	791	71	791	100	100	227	1	23	24	115
69	HCFMX35	209324 10/02/97	pSport1	79	1292	1	1292	160	160	228	1	21	22	106
70	HMSFS21	209324 10/02/97	Uni-ZAP XR	80	1283	1	1283	28	28	229	1	17	18	37

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
71	HMUAO21	209324 10/02/97	pCMVSport 3.0	81	708	245	708	289	289	230	1	25	26	67
72	HCHAR28	209324 10/02/97	pSport1	82	1464	325	1463	482	482	231	1	46	47	50
73	HLYDU25	209324 10/02/97	pSport1	83	616	1	616	250	250	232	1	22	23	40
74	HOEJH89	209324 10/02/97	Uni-ZAP XR	84	928	18	903	25	25	233	1	19	20	41
75	HPFDG48	209324 10/02/97	Uni-ZAP XR	85	723	165	700	283	283	234	1	18	19	47
76	HWTBM18	209324 10/02/97	Uni-ZAP XR	86	570	1	570	45	45	235	1	21	22	39
77	HCFOM18	209324 10/02/97	pSport1	87	639	1	639	28	28	236	1	20	21	63
78	HMWFO02	209324 10/02/97	Uni-Zap XR	88	708	1	708	20	20	237	1	38	39	60

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
79	HNGAV42	209324 10/02/97	Uni-ZAP XR	89	949	1	949	278	278	238	1	28	29	62
80	HL3AB91	209324 10/02/97	Uni-ZAP XR	90	1171	1	1171	158	158	239	1	21	22	56
81	HSDSE75	209324 10/02/97	pBluescript	91	1151	1	1151	160	160	240	1	18	19	181
82	HLMFD85	209324 10/02/97	Lambda ZAP II	92	714	1	714	33	33	241	1	27	28	70
83	HLQCJ74	209324 10/02/97	Lambda ZAP II	93	810	1	810	261	261	242	1	17	18	61
84	HLQCK07	209324 10/02/97	Lambda ZAP II	94	1176	1	1176	410	410	243	1	18	19	34
85	HTEFU65	209324 10/02/97	Uni-ZAP XR	95	1028	1	1028	231	231	244	1	24	25	46
86	HLYBF22	209324 10/02/97	pSport1	96	747	1	747	39	39	245	1	32	33	50

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
87	HMDAP35	209324 10/02/97	Uni-ZAP XR	97	628	1	628	70	70	246	1	21	22	50
88	HTOJK60	209324 10/02/97	Uni-ZAP XR	98	904	1	904	217	217	247	1	19	20	32
89	HWBCN75	209324 10/02/97	pCMVSport 3.0	99	576	1	576	184	184	248	1	34	35	48
90	HROAH06	209324 10/02/97	Uni-ZAP XR	100	713	1	713	29	29	249	1	43	44	115
91	HSAXA83	209324 10/02/97	Uni-ZAP XR	101	649	1	649	92	92	250	1	22	23	74
92	HSDJE10	209324 10/02/97	Uni-ZAP XR	102	697	1	697	157	157	251	1	21	22	62
93	HBAMA40	209324 10/02/97	pSport1	103	1288	1	1288	95	95	252	1	31	32	72
94	HBAMB34	209324 10/02/97	pSport1	104	1027	1	1027	87	87	253	1	35	36	48

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
95	HCWKC15	209324 10/02/97	ZAP Express	105	710	1	710	37	37	254	1	18	19	40
96	HDTDM65	209324 10/02/97	pCMVSport 2.0	106	530	1	530	159	159	255	1	40	41	53
97	HMMBF71	209324 10/02/97	pSport1	107	392	1	392	153	153	256	1	24	25	40
98	HPBDH41	209324 10/02/97	pBluescript SK-	108	991	288	991	373	373	257	1	15	16	41
99	HPBEN24	209324 10/02/97	pBluescript SK-	109	912	363	912	541	541	258	1	20	21	52
100	HCUIM65	209324 10/02/97	ZAP Express	110	875	331	736	557	557	259	1	27	28	47
101	HKNAA95	209324 10/02/97	pBluescript SK-	111	459	1	459	114	114	260	1	28	29	52
102	HKIYH57	209324 10/02/97	pBluescript	112	609	156	609	336	336	261	1	23	24	54

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
103	HBIBW67	209324 10/02/97	Uni-ZAP XR	113	1404	1	1404	685	685	262	1	33	34	38
104	HCFCU88	209324 10/02/97	pSport1	114	853	1	853	326	326	263	1	14	15	23
105	HBJMG49	209324 10/02/97	Uni-ZAP XR	115	845	1	804	53	53	264	1	17	18	46
106	H6EDC19	209324 10/02/97	Uni-ZAP XR	116	760	324	760	389	389	265	1	25	26	114
107	HSKHZ81	209346 10/09/97	pBluescript	117	988	1	967	57	57	266	1	27	28	247
108	HBJFX78	209346 10/09/97	Uni-ZAP XR	118	1947	1	1947	34	34	267	1	18	19	177
109	HEMFS60	209346 10/09/97	Uni-ZAP XR	119	1448	63	1448	111	111	268	1	17	18	78
110	HKACB56	209346 10/09/97	pCMVSport 2.0	120	496	1	496	27	27	269	1	23	24	80

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
111	HTXJX80	209346 10/09/97	Uni-ZAP XR	121	1174	16	880	206	206	270	1	26	27	68
112	HAFBD61	209346 10/09/97	pBluescript SK-	122	1046	1	1046	210	210	271	1	22	23	130
113	HBJJU28	209346 10/09/97	Uni-ZAP XR	123	1160	1	1160	133	133	272	1	18	19	84
114	HNHEI47	209346 10/09/97	Uni-ZAP XR	124	893	1	893	192	192	273	1	18	19	78
115	HPMFY74	209346 10/09/97	Uni-ZAP XR	125	1049	1	1049	91	91	274	1	40	41	53
116	HKACD58	209346 10/09/97	pCMVSport 2.0	126	1626	1	1626	35	35	275	1	25	26	154
117	HLDBB60	209346 10/09/97	pCMVSport 3.0	127	1177	1	1177	283	283	276	1	20	21	128
118	HLYAP91	209346 10/09/97	pSport1	128	1276	1	1276	280	280	277	1	29	30	83

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
119	HSKNB56	209346 10/09/97	pBluescript	129	1334	449	1334	484	484	278	1	25	26	85
120	HHGCW91	209346 10/09/97	Lambda ZAP II	130	532	1	532	107	107	279	1	18	19	95
121	HKIYE96	209346 10/09/97	pBluescript	131	685	145	685	284	284	280	1	19	20	97
122	HLYAN59	209346 10/09/97	pSport1	132	729	1	729	254	254	281	1	40	41	54
123	HNEEE24	209346 10/09/97	Uni-ZAP XR	133	1079	1	1079	213	213	282	1	21	22	71
124	HAPRK85	209346 10/09/97	Uni-ZAP XR	134	1297	1	1297	175	175	283	1	29	30	43
125	HLTEJ06	209346 10/09/97	Uni-ZAP XR	135	617	69	617	197	197	284	1	22	23	55
126	HMEKT48	209346 10/09/97	Lambda ZAP II	136	1311	1	1115	47	47	285	1	19	20	48

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
127	HNGHR74	209346 10/09/97	Uni-ZAP XR	137	1095	1	1095	53	53	286	1	18	19	41
128	HNHED17	209346 10/09/97	Uni-ZAP XR	138	692	1	692	282	282	287	1	19	20	48
129	HNHEP59	209346 10/09/97	Uni-ZAP XR	139	748	1	748	247	247	288	1	27	28	109
130	HNHFJ25	209346 10/09/97	Uni-ZAP XR	140	1132	1	1132	145	145	289	1	22	23	63
131	HCPAA69	209346 10/09/97	Uni-ZAP XR	141	1112	1	1112	8	8	290	1	20	21	41
132	HEAAR07	209346 10/09/97	Uni-ZAP XR	142	1084	1	1084	48	48	291	1	31	32	42
133	HHGDW43	209346 10/09/97	Lambda ZAP II	143	1050	1	1050	107	107	292	1	41	42	44
134	HHSDX28	209346 10/09/97	Uni-ZAP XR	144	1113	1	1113	90	90	293	1	21	22	56

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
135	HE8ER60	209346 10/09/97	Uni-ZAP XR	145	685	1	685	48	48	294	1	32	33	74
136	HMEJQ66	209346 10/09/97	Lambda ZAP II	146	1038	1	1038	80	80	295	1	24	25	50
137	HRDAD66	209346 10/09/97	Uni-ZAP XR	147	851	99	851	269	269	296	1	33	34	44
138	HCMST14	209346 10/09/97	Uni-ZAP XR	148	614	1	614	136	136	297	1	24	25	47
139	HCEBA03	209346 10/09/97	Uni-ZAP XR	149	1200	1	1200	76	76	298	1	21	22	54
140	HFAAH18	209346 10/09/97	Uni-ZAP XR	150	683	79	683	304	304	299	1	21	22	29
141	HJAAM10	209346 10/09/97	pBluescript SK-	151	827	135	827	320	320	300	1	35	36	72
142	HFIBV09	209346 10/09/97	pSport1	152	835	129	835	370	370	301	1	17	18	36

Gene No.	cDNA Clone ID	ATCC Deposit Nr and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
143	HOHCC74	209346 10/09/97	pCMVSport 2.0	153	558	1	558	327	327	302	1	20	21	48
144	HPMFY57	209346 10/09/97	Uni-ZAP XR	154	1201	1	1201	250	250	303	1	30	31	42
145	HFXDN63	209346 10/09/97	Lambda ZAP II	155	1026	1	1026	33	33	304	1	14	15	53
146	HADCL76	209346 10/09/97	pSport1	156	904	1	904	108	108	305	1	29	30	75
147	HMMAS76	209346 10/09/97	pSport1	157	916	1	916	13	13	306	1	29	30	62
148	HMKCG09	209346 10/09/97	pSport1	158	921	60	921	221	221	307	1	28	29	49

Table 1 summarizes the information corresponding to each "Gene No." described above. The nucleotide sequence identified as "NT SEQ ID NO:X" was assembled from partially homologous ("overlapping") sequences obtained from the "cDNA clone ID" identified in Table 1 and, in some cases, from additional related DNA clones. The overlapping sequences were assembled into a single contiguous sequence of high redundancy (usually three to five overlapping sequences at each nucleotide position), resulting in a final sequence identified as SEQ ID NO:X.

The cDNA Clone ID was deposited on the date and given the corresponding deposit number listed in "ATCC Deposit No:Z and Date." Some of the deposits contain multiple different clones corresponding to the same gene. "Vector" refers to the type of vector contained in the cDNA Clone ID.

"Total NT Seq." refers to the total number of nucleotides in the contig identified by "Gene No." The deposited clone may contain all or most of these sequences, reflected by the nucleotide position indicated as "5' NT of Clone Seq." and the "3' NT of Clone Seq." of SEQ ID NO:X. The nucleotide position of SEQ ID NO:X of the putative start codon (methionine) is identified as "5' NT of Start Codon." Similarly, the nucleotide position of SEQ ID NO:X of the predicted signal sequence is identified as "5' NT of First AA of Signal Pep."

The translated amino acid sequence, beginning with the methionine, is identified as "AA SEQ ID NO:Y," although other reading frames can also be easily translated using known molecular biology techniques. The polypeptides produced by these alternative open reading frames are specifically contemplated by the present invention.

The first and last amino acid position of SEQ ID NO:Y of the predicted signal peptide is identified as "First AA of Sig Pep" and "Last AA of Sig Pep." The predicted first amino acid position of SEQ ID NO:Y of the secreted portion is identified as "Predicted First AA of Secreted Portion." Finally, the amino acid position of SEQ ID NO:Y of the last amino acid in the open reading frame is identified as "Last AA of ORF."

SEQ ID NO:X and the translated SEQ ID NO:Y are sufficiently accurate and otherwise suitable for a variety of uses well known in the art and described further below. For instance, SEQ ID NO:X is useful for designing nucleic acid hybridization probes that will detect nucleic acid sequences contained in SEQ ID NO:X or the cDNA contained in the deposited clone. These probes will also hybridize to nucleic acid molecules in biological samples, thereby enabling a variety of forensic and diagnostic methods of the invention. Similarly, polypeptides identified from SEQ ID NO:Y may be used to generate antibodies which bind specifically to the secreted proteins encoded by the cDNA clones identified in Table 1.

Nevertheless, DNA sequences generated by sequencing reactions can contain sequencing errors. The errors exist as misidentified nucleotides, or as insertions or deletions of nucleotides in the generated DNA sequence. The erroneously inserted or deleted nucleotides cause frame shifts in the reading frames of the predicted amino acid sequence. In these cases, the predicted amino acid sequence diverges from the actual amino acid sequence, even though the generated DNA sequence may be greater than 99.9% identical to the actual DNA sequence (for example, one base insertion or deletion in an open reading frame of over 1000 bases).

Accordingly, for those applications requiring precision in the nucleotide sequence or the amino acid sequence, the present invention provides not only the generated nucleotide sequence identified as SEQ ID NO:X and the predicted translated amino acid sequence identified as SEQ ID NO:Y, but also a sample of plasmid DNA containing a human cDNA of the invention deposited with the ATCC, as set forth in Table 1. The nucleotide sequence of each deposited clone can readily be determined by sequencing the deposited clone in accordance with known methods. The predicted amino acid sequence can then be verified from such deposits. Moreover, the amino acid sequence of the protein encoded by a particular clone can also be directly determined by peptide sequencing or by expressing the protein in a suitable host cell containing the deposited human cDNA, collecting the protein, and determining its sequence.

The present invention also relates to the genes corresponding to SEQ ID NO:X, SEQ ID NO:Y, or the deposited clone. The corresponding gene can be isolated in accordance with known methods using the sequence information disclosed herein. Such methods include preparing probes or primers from the disclosed sequence and identifying or amplifying the corresponding gene from appropriate sources of genomic material.

Also provided in the present invention are species homologs. Species homologs may be isolated and identified by making suitable probes or primers from the sequences provided herein and screening a suitable nucleic acid source for the desired homologue.

The polypeptides of the invention can be prepared in any suitable manner. Such polypeptides include isolated naturally occurring polypeptides, recombinantly produced polypeptides, synthetically produced polypeptides, or polypeptides produced by a combination of these methods. Means for preparing such polypeptides are well understood in the art.

The polypeptides may be in the form of the secreted protein, including the mature form, or may be a part of a larger protein, such as a fusion protein (see below).

It is often advantageous to include an additional amino acid sequence which contains secretory or leader sequences, pro-sequences, sequences which aid in purification , such as multiple histidine residues, or an additional sequence for stability during recombinant production.

The polypeptides of the present invention are preferably provided in an isolated form, and preferably are substantially purified. A recombinantly produced version of a polypeptide, including the secreted polypeptide, can be substantially purified by the one-step method described in Smith and Johnson, Gene 67:31-40 (1988). Polypeptides of the invention also can be purified from natural or recombinant sources using antibodies of the invention raised against the secreted protein in methods which are well known in the art.

Signal Sequences

Methods for predicting whether a protein has a signal sequence, as well as the cleavage point for that sequence, are available. For instance, the method of McGeoch, Virus Res. 3:271-286 (1985), uses the information from a short N-terminal charged region and a subsequent uncharged region of the complete (uncleaved) protein. The method of von Heinje, Nucleic Acids Res. 14:4683-4690 (1986) uses the information from the residues surrounding the cleavage site, typically residues -13 to +2, where +1 indicates the amino terminus of the secreted protein. The accuracy of predicting the cleavage points of known mammalian secretory proteins for each of these methods is in the range of 75-80%. (von Heinje, supra.) However, the two methods do not always produce the same predicted cleavage point(s) for a given protein.

In the present case, the deduced amino acid sequence of the secreted polypeptide was analyzed by a computer program called SignalP (Henrik Nielsen et al., Protein Engineering 10:1-6 (1997)), which predicts the cellular location of a protein based on the amino acid sequence. As part of this computational prediction of localization, the methods of McGeoch and von Heinje are incorporated. The analysis of the amino acid sequences of the secreted proteins described herein by this program provided the results shown in Table 1.

As one of ordinary skill would appreciate, however, cleavage sites sometimes vary from organism to organism and cannot be predicted with absolute certainty. Accordingly, the present invention provides secreted polypeptides having a sequence shown in SEQ ID NO:Y which have an N-terminus beginning within 5 residues (i.e., + or - 5 residues) of the predicted cleavage point. Similarly, it is also recognized that in some cases, cleavage of the signal sequence from a secreted protein is not entirely

uniform, resulting in more than one secreted species. These polypeptides, and the polynucleotides encoding such polypeptides, are contemplated by the present invention.

Moreover, the signal sequence identified by the above analysis may not necessarily predict the naturally occurring signal sequence. For example, the naturally occurring signal sequence may be further upstream from the predicted signal sequence. However, it is likely that the predicted signal sequence will be capable of directing the secreted protein to the ER. These polypeptides, and the polynucleotides encoding such polypeptides, are contemplated by the present invention.

Polynucleotide and Polypeptide Variants

"Variant" refers to a polynucleotide or polypeptide differing from the polynucleotide or polypeptide of the present invention, but retaining essential properties thereof. Generally, variants are overall closely similar, and, in many regions, identical to the polynucleotide or polypeptide of the present invention.

By a polynucleotide having a nucleotide sequence at least, for example, 95% "identical" to a reference nucleotide sequence of the present invention, it is intended that the nucleotide sequence of the polynucleotide is identical to the reference sequence except that the polynucleotide sequence may include up to five point mutations per each 100 nucleotides of the reference nucleotide sequence encoding the polypeptide. In other words, to obtain a polynucleotide having a nucleotide sequence at least 95% identical to a reference nucleotide sequence, up to 5% of the nucleotides in the reference sequence may be deleted or substituted with another nucleotide, or a number of nucleotides up to 5% of the total nucleotides in the reference sequence may be inserted into the reference sequence. The query sequence may be an entire sequence shown inTable 1, the ORF (open reading frame), or any fragement specified as described herein.

As a practical matter, whether any particular nucleic acid molecule or polypeptide is at least 90%, 95%, 96%, 97%, 98% or 99% identical to a nucleotide sequence of the presence invention can be determined conventionally using known computer programs. A preferred method for determing the best overall match between a query sequence (a sequence of the present invention) and a subject sequence, also referred to as a global sequence alignment, can be determined using the FASTDB computer program based on the algorithm of Brutlag et al. (Comp. App. Biosci. (1990) 6:237-245). In a sequence alignment the query and subject sequences are both DNA sequences. An RNA sequence can be compared by converting U's to T's. The result of said global sequence alignment is in percent identity. Preferred parameters used in a FASTDB alignment of DNA sequences to calculate percent identiy are: Matrix=Unitary, k-tuple=4, Mismatch Penalty=1, Joining Penalty=30, Randomization

Group Length=0, Cutoff Score=1, Gap Penalty=5, Gap Size Penalty 0.05, Window Size=500 or the lenght of the subject nucleotide sequence, whichever is shorter.

If the subject sequence is shorter than the query sequence because of 5' or 3' deletions, not because of internal deletions, a manual correction must be made to the results. This is becuase the FASTDB program does not account for 5' and 3' truncations of the subject sequence when calculating percent identity. For subject sequences truncated at the 5' or 3' ends, relative to the the query sequence, the percent identity is corrected by calculating the number of bases of the query sequence that are 5' and 3' of the subject sequence, which are not matched/aligned, as a percent of the total bases of the query sequence. Whether a nucleotide is matched/aligned is determined by results of the FASTDB sequence alignment. This percentage is then subtracted from the percent identity, calculated by the above FASTDB program using the specified parameters, to arrive at a final percent identity score. This corrected score is what is used for the purposes of the present invention. Only bases outside the 5' and 3' bases of the subject sequence, as displayed by the FASTDB alignment, which are not matched/aligned with the query sequence, are calculated for the purposes of manually adjusting the percent identity score.

For example, a 90 base subject sequence is aligned to a 100 base query sequence to determine percent identity. The deletions occur at the 5' end of the subject sequence and therefore, the FASTDB alignment does not show a matched/alignement of the first 10 bases at 5' end. The 10 unpaired bases represent 10% of the sequence (number of bases at the 5' and 3' ends not matched/total number of bases in the query sequence) so 10% is subtracted from the percent identity score calculated by the FASTDB program. If the remaining 90 bases were perfectly matched the final percent identity would be 90%. In another example, a 90 base subject sequence is compared with a 100 base query sequence. This time the deletions are internal deletions so that there are no bases on the 5' or 3' of the subject sequence which are not matched/aligned with the query. In this case the percent identity calculated by FASTDB is not manually corrected. Once again, only bases 5' and 3' of the subject sequence which are not matched/aligned with the query sequnce are manually corrected for. No other manual corrections are to made for the purposes of the present invention.

By a polypeptide having an amino acid sequence at least, for example, 95% "identical" to a query amino acid sequence of the present invention, it is intended that the amino acid sequence of the subject polypeptide is identical to the query sequence except that the subject polypeptide sequence may include up to five amino acid alterations per each 100 amino acids of the query amino acid sequence. In other words, to obtain a polypeptide having an amino acid sequence at least 95% identical to a query

amino acid sequence, up to 5% of the amino acid residues in the subject sequence may be inserted, deleted, (indels) or substituted with another amino acid. These alterations of the reference sequence may occur at the amino or carboxy terminal positions of the reference amino acid sequence or anywhere between those terminal positions, interspersed either individually among residues in the reference sequence or in one or more contiguous groups within the reference sequence.

As a practical matter, whether any particular polypeptide is at least 90%, 95%, 96%, 97%, 98% or 99% identical to, for instance, the amino acid sequences shown in Table 1 or to the amino acid sequence encoded by deposited DNA clone can be determined conventionally using known computer programs. A preferred method for determing the best overall match between a query sequence (a sequence of the present invention) and a subject sequence, also referred to as a global sequence alignment, can be determined using the FASTDB computer program based on the algorithm of Brutlag et al. (Comp. App. Biosci. (1990) 6:237-245). In a sequence alignment the query and subject sequences are either both nucleotide sequences or both amino acid sequences. The result of said global sequence alignment is in percent identity. Preferred parameters used in a FASTDB amino acid alignment are: Matrix=PAM 0, k-tuple=2, Mismatch Penalty=1, Joining Penalty=20, Randomization Group Length=0, Cutoff Score=1, Window Size=sequence length, Gap Penalty=5, Gap Size Penalty=0.05, Window Size=500 or the length of the subject amino acid sequence, whichever is shorter.

If the subject sequence is shorter than the query sequence due to N- or C-terminal deletions, not because of internal deletions, a manual correction must be made to the results. This is becuase the FASTDB program does not account for N- and C-terminal truncations of the subject sequence when calculating global percent identity. For subject sequences truncated at the N- and C-termini, relative to the the query sequence, the percent identity is corrected by calculating the number of residues of the query sequence that are N- and C-terminal of the subject sequence, which are not matched/aligned with a corresponding subject residue, as a percent of the total bases of the query sequence. Whether a residue is matched/aligned is determined by results of the FASTDB sequence alignment. This percentage is then subtracted from the percent identity, calculated by the above FASTDB program using the specified parameters, to arrive at a final percent identity score. This final percent identity score is what is used for the purposes of the present invention. Only residues to the N- and C-termini of the subject sequence, which are not matched/aligned with the query sequence, are considered for the purposes of manually adjusting the percent identity score. That is, only query residue positions outside the farthest N- and C-terminal residues of the subject sequence.

For example, a 90 amino acid residue subject sequence is aligned with a 100 residue query sequence to determine percent identity. The deletion occurs at the N-terminus of the subject sequence and therefore, the FASTDB alignment does not show a matching/alignment of the first 10 residues at the N-terminus. The 10 unpaired residues represent 10% of the sequence (number of residues at the N- and C- termini not matched/total number of residues in the query sequence) so 10% is subtracted from the percent identity score calculated by the FASTDB program. If the remaining 90 residues were perfectly matched the final percent identity would be 90%. In another example, a 90 residue subject sequence is compared with a 100 residue query sequence. This time the deletions are internal deletions so there are no residues at the N- or C-termini of the subject sequence which are not matched/aligned with the query. In this case the percent identity calculated by FASTDB is not manually corrected. Once again, only residue positions outside the N- and C-terminal ends of the subject sequence, as displayed in the FASTDB alignment, which are not matched/aligned with the query sequnce are manually corrected for. No other manual corrections are to made for the purposes of the present invention.

The variants may contain alterations in the coding regions, non-coding regions, or both. Especially preferred are polynucleotide variants containing alterations which produce silent substitutions, additions, or deletions, but do not alter the properties or activities of the encoded polypeptide. Nucleotide variants produced by silent substitutions due to the degeneracy of the genetic code are preferred. Moreover, variants in which 5-10, 1-5, or 1-2 amino acids are substituted, deleted, or added in any combination are also preferred. Polynucleotide variants can be produced for a variety of reasons, e.g., to optimize codon expression for a particular host (change codons in the human mRNA to those preferred by a bacterial host such as E. coli).

Naturally occurring variants are called "allelic variants," and refer to one of several alternate forms of a gene occupying a given locus on a chromosome of an organism. (Genes II, Lewin, B., ed., John Wiley & Sons, New York (1985).) These allelic variants can vary at either the polynucleotide and/or polypeptide level. Alternatively, non-naturally occurring variants may be produced by mutagenesis techniques or by direct synthesis.

Using known methods of protein engineering and recombinant DNA technology, variants may be generated to improve or alter the characteristics of the polypeptides of the present invention. For instance, one or more amino acids can be deleted from the N-terminus or C-terminus of the secreted protein without substantial loss of biological function. The authors of Ron et al., J. Biol. Chem. 268: 2984-2988 (1993), reported variant KGF proteins having heparin binding activity even after

deleting 3, 8, or 27 amino-terminal amino acid residues. Similarly, Interferon gamma exhibited up to ten times higher activity after deleting 8-10 amino acid residues from the carboxy terminus of this protein. (Dobeli et al., J. Biotechnology 7:199-216 (1988).)

Moreover, ample evidence demonstrates that variants often retain a biological activity similar to that of the naturally occurring protein. For example, Gayle and coworkers (J. Biol. Chem 268:22105-22111 (1993)) conducted extensive mutational analysis of human cytokine IL-1a. They used random mutagenesis to generate over 3,500 individual IL-1a mutants that averaged 2.5 amino acid changes per variant over the entire length of the molecule. Multiple mutations were examined at every possible amino acid position. The investigators found that "[m]ost of the molecule could be altered with little effect on either [binding or biological activity]." (See, Abstract.) In fact, only 23 unique amino acid sequences, out of more than 3,500 nucleotide sequences examined, produced a protein that significantly differed in activity from wild-type.

Furthermore, even if deleting one or more amino acids from the N-terminus or C-terminus of a polypeptide results in modification or loss of one or more biological functions, other biological activities may still be retained. For example, the ability of a deletion variant to induce and/or to bind antibodies which recognize the secreted form will likely be retained when less than the majority of the residues of the secreted form are removed from the N-terminus or C-terminus. Whether a particular polypeptide lacking N- or C-terminal residues of a protein retains such immunogenic activities can readily be determined by routine methods described herein and otherwise known in the art.

Thus, the invention further includes polypeptide variants which show substantial biological activity. Such variants include deletions, insertions, inversions, repeats, and substitutions selected according to general rules known in the art so as have little effect on activity. For example, guidance concerning how to make phenotypically silent amino acid substitutions is provided in Bowie, J. U. et al., Science 247:1306-1310 (1990), wherein the authors indicate that there are two main strategies for studying the tolerance of an amino acid sequence to change.

The first strategy exploits the tolerance of amino acid substitutions by natural selection during the process of evolution. By comparing amino acid sequences in different species, conserved amino acids can be identified. These conserved amino acids are likely important for protein function. In contrast, the amino acid positions where substitutions have been tolerated by natural selection indicates that these positions are not critical for protein function. Thus, positions tolerating amino acid substitution could be modified while still maintaining biological activity of the protein.

The second strategy uses genetic engineering to introduce amino acid changes at specific positions of a cloned gene to identify regions critical for protein function. For example, site directed mutagenesis or alanine-scanning mutagenesis (introduction of single alanine mutations at every residue in the molecule) can be used. (Cunningham and Wells, Science 244:1081-1085 (1989).) The resulting mutant molecules can then be tested for biological activity.

As the authors state, these two strategies have revealed that proteins are surprisingly tolerant of amino acid substitutions. The authors further indicate which amino acid changes are likely to be permissive at certain amino acid positions in the protein. For example, most buried (within the tertiary structure of the protein) amino acid residues require nonpolar side chains, whereas few features of surface side chains are generally conserved. Moreover, tolerated conservative amino acid substitutions involve replacement of the aliphatic or hydrophobic amino acids Ala, Val, Leu and Ile; replacement of the hydroxyl residues Ser and Thr; replacement of the acidic residues Asp and Glu; replacement of the amide residues Asn and Gln, replacement of the basic residues Lys, Arg, and His; replacement of the aromatic residues Phe, Tyr, and Trp, and replacement of the small-sized amino acids Ala, Ser, Thr, Met, and Gly.

Besides conservative amino acid substitution, variants of the present invention include (i) substitutions with one or more of the non-conserved amino acid residues, where the substituted amino acid residues may or may not be one encoded by the genetic code, or (ii) substitution with one or more of amino acid residues having a substituent group, or (iii) fusion of the mature polypeptide with another compound, such as a compound to increase the stability and/or solubility of the polypeptide (for example, polyethylene glycol), or (iv) fusion of the polypeptide with additional amino acids, such as an IgG Fc fusion region peptide, or leader or secretory sequence, or a sequence facilitating purification. Such variant polypeptides are deemed to be within the scope of those skilled in the art from the teachings herein.

For example, polypeptide variants containing amino acid substitutions of charged amino acids with other charged or neutral amino acids may produce proteins with improved characteristics, such as less aggregation. Aggregation of pharmaceutical formulations both reduces activity and increases clearance due to the aggregate's immunogenic activity. (Pinckard et al., Clin. Exp. Immunol. 2:331-340 (1967); Robbins et al., Diabetes 36: 838-845 (1987); Cleland et al., Crit. Rev. Therapeutic Drug Carrier Systems 10:307-377 (1993).)

Polynucleotide and Polypeptide Fragments

In the present invention, a "polynucleotide fragment" refers to a short polynucleotide having a nucleic acid sequence contained in the deposited clone or shown in SEQ ID NO:X. The short nucleotide fragments are preferably at least about 15 nt, and more preferably at least about 20 nt, still more preferably at least about 30 nt, and even more preferably, at least about 40 nt in length. A fragment "at least 20 nt in length," for example, is intended to include 20 or more contiguous bases from the cDNA sequence contained in the deposited clone or the nucleotide sequence shown in SEQ ID NO:X. These nucleotide fragments are useful as diagnostic probes and primers as discussed herein. Of course, larger fragments (e.g., 50, 150, 500, 600, 2000 nucleotides) are preferred.

Moreover, representative examples of polynucleotide fragments of the invention, include, for example, fragments having a sequence from about nucleotide number 1-50, 51-100, 101-150, 151-200, 201-250, 251-300, 301-350, 351-400, 401-450, 451-500, 501-550, 551-600, 651-700, 701-750, 751-800, 800-850, 851-900, 901-950, 951-1000, 1001-1050, 1051-1100, 1101-1150, 1151-1200, 1201-1250, 1251-1300, 1301-1350, 1351-1400, 1401-1450, 1451-1500, 1501-1550, 1551-1600, 1601-1650, 1651-1700, 1701-1750, 1751-1800, 1801-1850, 1851-1900, 1901-1950, 1951-2000, or 2001 to the end of SEQ ID NO:X or the cDNA contained in the deposited clone. In this context "about" includes the particularly recited ranges, larger or smaller by several (5, 4, 3, 2, or 1) nucleotides, at either terminus or at both termini. Preferably, these fragments encode a polypeptide which has biological activity. More preferably, these polynucleotides can be used as probes or primers as discussed herein.

In the present invention, a "polypeptide fragment" refers to a short amino acid sequence contained in SEQ ID NO:Y or encoded by the cDNA contained in the deposited clone. Protein fragments may be "free-standing," or comprised within a larger polypeptide of which the fragment forms a part or region, most preferably as a single continuous region. Representative examples of polypeptide fragments of the invention, include, for example, fragments from about amino acid number 1-20, 21-40, 41-60, 61-80, 81-100, 102-120, 121-140, 141-160, or 161 to the end of the coding region. Moreover, polypeptide fragments can be about 20, 30, 40, 50, 60, 70, 80, 90, 100, 110, 120, 130, 140, or 150 amino acids in length. In this context "about" includes the particularly recited ranges, larger or smaller by several (5, 4, 3, 2, or 1) amino acids, at either extreme or at both extremes.

Preferred polypeptide fragments include the secreted protein as well as the mature form. Further preferred polypeptide fragments include the secreted protein or the mature form having a continuous series of deleted residues from the amino or the carboxy terminus, or both. For example, any number of amino acids, ranging from 1-

60, can be deleted from the amino terminus of either the secreted polypeptide or the mature form. Similarly, any number of amino acids, ranging from 1-30, can be deleted from the carboxy terminus of the secreted protein or mature form. Furthermore, any combination of the above amino and carboxy terminus deletions are preferred. Similarly, polynucleotide fragments encoding these polypeptide fragments are also preferred.

Also preferred are polypeptide and polynucleotide fragments characterized by structural or functional domains, such as fragments that comprise alpha-helix and alpha-helix forming regions, beta-sheet and beta-sheet-forming regions, turn and turn-forming regions, coil and coil-forming regions, hydrophilic regions, hydrophobic regions, alpha amphipathic regions, beta amphipathic regions, flexible regions, surface-forming regions, substrate binding region, and high antigenic index regions. Polypeptide fragments of SEQ ID NO:Y falling within conserved domains are specifically contemplated by the present invention. Moreover, polynucleotide fragments encoding these domains are also contemplated.

Other preferred fragments are biologically active fragments. Biologically active fragments are those exhibiting activity similar, but not necessarily identical, to an activity of the polypeptide of the present invention. The biological activity of the fragments may include an improved desired activity, or a decreased undesirable activity.

Epitopes & Antibodies

In the present invention, "epitopes" refer to polypeptide fragments having antigenic or immunogenic activity in an animal, especially in a human. A preferred embodiment of the present invention relates to a polypeptide fragment comprising an epitope, as well as the polynucleotide encoding this fragment. A region of a protein molecule to which an antibody can bind is defined as an "antigenic epitope." In contrast, an "immunogenic epitope" is defined as a part of a protein that elicits an antibody response. (See, for instance, Geysen et al., Proc. Natl. Acad. Sci. USA 81:3998- 4002 (1983).)

Fragments which function as epitopes may be produced by any conventional means. (See, e.g., Houghten, R. A., Proc. Natl. Acad. Sci. USA 82:5131-5135 (1985) further described in U.S. Patent No. 4,631,211.)

In the present invention, antigenic epitopes preferably contain a sequence of at least seven, more preferably at least nine, and most preferably between about 15 to about 30 amino acids. Antigenic epitopes are useful to raise antibodies, including monoclonal antibodies, that specifically bind the epitope. (See, for instance, Wilson et al., Cell 37:767-778 (1984); Sutcliffe, J. G. et al., Science 219:660-666 (1983).)

Similarly, immunogenic epitopes can be used to induce antibodies according to methods well known in the art. (See, for instance, Sutcliffe et al., supra; Wilson et al., supra; Chow, M. et al., Proc. Natl. Acad. Sci. USA 82:910-914; and Bittle, F. J. et al., J. Gen. Virol. 66:2347-2354 (1985).) A preferred immunogenic epitope includes the secreted protein. The immunogenic epitopes may be presented together with a carrier protein, such as an albumin, to an animal system (such as rabbit or mouse) or, if it is long enough (at least about 25 amino acids), without a carrier. However, immunogenic epitopes comprising as few as 8 to 10 amino acids have been shown to be sufficient to raise antibodies capable of binding to, at the very least, linear epitopes in a denatured polypeptide (e.g., in Western blotting.)

As used herein, the term "antibody" (Ab) or "monoclonal antibody" (Mab) is meant to include intact molecules as well as antibody fragments (such as, for example, Fab and F(ab')2 fragments) which are capable of specifically binding to protein. Fab and F(ab')2 fragments lack the Fc fragment of intact antibody, clear more rapidly from the circulation, and may have less non-specific tissue binding than an intact antibody. (Wahl et al., J. Nucl. Med. 24:316-325 (1983).) Thus, these fragments are preferred, as well as the products of a FAB or other immunoglobulin expression library. Moreover, antibodies of the present invention include chimeric, single chain, and humanized antibodies.

Fusion Proteins

Any polypeptide of the present invention can be used to generate fusion proteins. For example, the polypeptide of the present invention, when fused to a second protein, can be used as an antigenic tag. Antibodies raised against the polypeptide of the present invention can be used to indirectly detect the second protein by binding to the polypeptide. Moreover, because secreted proteins target cellular locations based on trafficking signals, the polypeptides of the present invention can be used as targeting molecules once fused to other proteins.

Examples of domains that can be fused to polypeptides of the present invention include not only heterologous signal sequences, but also other heterologous functional regions. The fusion does not necessarily need to be direct, but may occur through linker sequences.

Moreover, fusion proteins may also be engineered to improve characteristics of the polypeptide of the present invention. For instance, a region of additional amino acids, particularly charged amino acids, may be added to the N-terminus of the polypeptide to improve stability and persistence during purification from the host cell or subsequent handling and storage. Also, peptide moieties may be added to the

polypeptide to facilitate purification. Such regions may be removed prior to final preparation of the polypeptide. The addition of peptide moieties to facilitate handling of polypeptides are familiar and routine techniques in the art.

Moreover, polypeptides of the present invention, including fragments, and specifically epitopes, can be combined with parts of the constant domain of immunoglobulins (IgG), resulting in chimeric polypeptides. These fusion proteins facilitate purification and show an increased half-life in vivo. One reported example describes chimeric proteins consisting of the first two domains of the human CD4-polypeptide and various domains of the constant regions of the heavy or light chains of mammalian immunoglobulins. (EP A 394,827; Traunecker et al., Nature 331:84-86 (1988).) Fusion proteins having disulfide-linked dimeric structures (due to the IgG) can also be more efficient in binding and neutralizing other molecules, than the monomeric secreted protein or protein fragment alone. (Fountoulakis et al., J. Biochem. 270:3958-3964 (1995).)

Similarly, EP-A-O 464 533 (Canadian counterpart 2045869) discloses fusion proteins comprising various portions of constant region of immunoglobulin molecules together with another human protein or part thereof. In many cases, the Fc part in a fusion protein is beneficial in therapy and diagnosis, and thus can result in, for example, improved pharmacokinetic properties. (EP-A 0232 262.) Alternatively, deleting the Fc part after the fusion protein has been expressed, detected, and purified, would be desired. For example, the Fc portion may hinder therapy and diagnosis if the fusion protein is used as an antigen for immunizations. In drug discovery, for example, human proteins, such as hIL-5, have been fused with Fc portions for the purpose of high-throughput screening assays to identify antagonists of hIL-5. (See, D. Bennett et al., J. Molecular Recognition 8:52-58 (1995); K. Johanson et al., J. Biol. Chem. 270:9459-9471 (1995).)

Moreover, the polypeptides of the present invention can be fused to marker sequences, such as a peptide which facilitates purification of the fused polypeptide. In preferred embodiments, the marker amino acid sequence is a hexa-histidine peptide, such as the tag provided in a pQE vector (QIAGEN, Inc., 9259 Eton Avenue, Chatsworth, CA, 91311), among others, many of which are commercially available. As described in Gentz et al., Proc. Natl. Acad. Sci. USA 86:821-824 (1989), for instance, hexa-histidine provides for convenient purification of the fusion protein. Another peptide tag useful for purification, the "HA" tag, corresponds to an epitope derived from the influenza hemagglutinin protein. (Wilson et al., Cell 37:767 (1984).)

Thus, any of these above fusions can be engineered using the polynucleotides or the polypeptides of the present invention.

Vectors, Host Cells, and Protein Production

The present invention also relates to vectors containing the polynucleotide of the present invention, host cells, and the production of polypeptides by recombinant techniques. The vector may be, for example, a phage, plasmid, viral, or retroviral vector. Retroviral vectors may be replication competent or replication defective. In the latter case, viral propagation generally will occur only in complementing host cells.

The polynucleotides may be joined to a vector containing a selectable marker for propagation in a host. Generally, a plasmid vector is introduced in a precipitate, such as a calcium phosphate precipitate, or in a complex with a charged lipid. If the vector is a virus, it may be packaged in vitro using an appropriate packaging cell line and then transduced into host cells.

The polynucleotide insert should be operatively linked to an appropriate promoter, such as the phage lambda PL promoter, the E. coli lac, trp, phoA and tac promoters, the SV40 early and late promoters and promoters of retroviral LTRs, to name a few. Other suitable promoters will be known to the skilled artisan. The expression constructs will further contain sites for transcription initiation, termination, and, in the transcribed region, a ribosome binding site for translation. The coding portion of the transcripts expressed by the constructs will preferably include a translation initiating codon at the beginning and a termination codon (UAA, UGA or UAG) appropriately positioned at the end of the polypeptide to be translated.

As indicated, the expression vectors will preferably include at least one selectable marker. Such markers include dihydrofolate reductase, G418 or neomycin resistance for eukaryotic cell culture and tetracycline, kanamycin or ampicillin resistance genes for culturing in E. coli and other bacteria. Representative examples of appropriate hosts include, but are not limited to, bacterial cells, such as E. coli, Streptomyces and Salmonella typhimurium cells; fungal cells, such as yeast cells; insect cells such as Drosophila S2 and Spodoptera Sf9 cells; animal cells such as CHO, COS, 293, and Bowes melanoma cells; and plant cells. Appropriate culture mediums and conditions for the above-described host cells are known in the art.

Among vectors preferred for use in bacteria include pQE70, pQE60 and pQE-9, available from QIAGEN, Inc.; pBluescript vectors, Phagescript vectors, pNH8A, pNH16a, pNH18A, pNH46A, available from Stratagene Cloning Systems, Inc.; and ptrc99a, pKK223-3, pKK233-3, pDR540, pRIT5 available from Pharmacia Biotech, Inc. Among preferred eukaryotic vectors are pWLNEO, pSV2CAT, pOG44, pXT1 and pSG available from Stratagene; and pSVK3, pBPV, pMSG and pSVL available from Pharmacia. Other suitable vectors will be readily apparent to the skilled artisan.

Introduction of the construct into the host cell can be effected by calcium phosphate transfection, DEAE-dextran mediated transfection, cationic lipid-mediated transfection, electroporation, transduction, infection, or other methods. Such methods are described in many standard laboratory manuals, such as Davis et al., Basic Methods In Molecular Biology (1986). It is specifically contemplated that the polypeptides of the present invention may in fact be expressed by a host cell lacking a recombinant vector.

A polypeptide of this invention can be recovered and purified from recombinant cell cultures by well-known methods including ammonium sulfate or ethanol precipitation, acid extraction, anion or cation exchange chromatography, phosphocellulose chromatography, hydrophobic interaction chromatography, affinity chromatography, hydroxylapatite chromatography and lectin chromatography. Most preferably, high performance liquid chromatography ("HPLC") is employed for purification.

Polypeptides of the present invention, and preferably the secreted form, can also be recovered from: products purified from natural sources, including bodily fluids, tissues and cells, whether directly isolated or cultured; products of chemical synthetic procedures; and products produced by recombinant techniques from a prokaryotic or eukaryotic host, including, for example, bacterial, yeast, higher plant, insect, and mammalian cells. Depending upon the host employed in a recombinant production procedure, the polypeptides of the present invention may be glycosylated or may be non-glycosylated. In addition, polypeptides of the invention may also include an initial modified methionine residue, in some cases as a result of host-mediated processes. Thus, it is well known in the art that the N-terminal methionine encoded by the translation initiation codon generally is removed with high efficiency from any protein after translation in all eukaryotic cells. While the N-terminal methionine on most proteins also is efficiently removed in most prokaryotes, for some proteins, this prokaryotic removal process is inefficient, depending on the nature of the amino acid to which the N-terminal methionine is covalently linked.

Uses of the Polynucleotides

Each of the polynucleotides identified herein can be used in numerous ways as reagents. The following description should be considered exemplary and utilizes known techniques.

The polynucleotides of the present invention are useful for chromosome identification. There exists an ongoing need to identify new chromosome markers, since few chromosome marking reagents, based on actual sequence data (repeat

polymorphisms), are presently available. Each polynucleotide of the present invention can be used as a chromosome marker.

Briefly, sequences can be mapped to chromosomes by preparing PCR primers (preferably 15-25 bp) from the sequences shown in SEQ ID NO:X. Primers can be selected using computer analysis so that primers do not span more than one predicted exon in the genomic DNA. These primers are then used for PCR screening of somatic cell hybrids containing individual human chromosomes. Only those hybrids containing the human gene corresponding to the SEQ ID NO:X will yield an amplified fragment.

Similarly, somatic hybrids provide a rapid method of PCR mapping the polynucleotides to particular chromosomes. Three or more clones can be assigned per day using a single thermal cycler. Moreover, sublocalization of the polynucleotides can be achieved with panels of specific chromosome fragments. Other gene mapping strategies that can be used include in situ hybridization, prescreening with labeled flow-sorted chromosomes, and preselection by hybridization to construct chromosome specific-cDNA libraries.

Precise chromosomal location of the polynucleotides can also be achieved using fluorescence in situ hybridization (FISH) of a metaphase chromosomal spread. This technique uses polynucleotides as short as 500 or 600 bases; however, polynucleotides 2,000-4,000 bp are preferred. For a review of this technique, see Verma et al., "Human Chromosomes: a Manual of Basic Techniques," Pergamon Press, New York (1988).

For chromosome mapping, the polynucleotides can be used individually (to mark a single chromosome or a single site on that chromosome) or in panels (for marking multiple sites and/or multiple chromosomes). Preferred polynucleotides correspond to the noncoding regions of the cDNAs because the coding sequences are more likely conserved within gene families, thus increasing the chance of cross hybridization during chromosomal mapping.

Once a polynucleotide has been mapped to a precise chromosomal location, the physical position of the polynucleotide can be used in linkage analysis. Linkage analysis establishes coinheritance between a chromosomal location and presentation of a particular disease. (Disease mapping data are found, for example, in V. McKusick, Mendelian Inheritance in Man (available on line through Johns Hopkins University Welch Medical Library) .) Assuming 1 megabase mapping resolution and one gene per 20 kb, a cDNA precisely localized to a chromosomal region associated with the disease could be one of 50-500 potential causative genes.

Thus, once coinheritance is established, differences in the polynucleotide and the corresponding gene between affected and unaffected individuals can be examined.

First, visible structural alterations in the chromosomes, such as deletions or translocations, are examined in chromosome spreads or by PCR. If no structural alterations exist, the presence of point mutations are ascertained. Mutations observed in some or all affected individuals, but not in normal individuals, indicates that the mutation may cause the disease. However, complete sequencing of the polypeptide and the corresponding gene from several normal individuals is required to distinguish the mutation from a polymorphism. If a new polymorphism is identified, this polymorphic polypeptide can be used for further linkage analysis.

Furthermore, increased or decreased expression of the gene in affected individuals as compared to unaffected individuals can be assessed using polynucleotides of the present invention. Any of these alterations (altered expression, chromosomal rearrangement, or mutation) can be used as a diagnostic or prognostic marker.

In addition to the foregoing, a polynucleotide can be used to control gene expression through triple helix formation or antisense DNA or RNA. Both methods rely on binding of the polynucleotide to DNA or RNA. For these techniques, preferred polynucleotides are usually 20 to 40 bases in length and complementary to either the region of the gene involved in transcription (triple helix - see Lee et al., Nucl. Acids Res. 6:3073 (1979); Cooney et al., Science 241:456 (1988); and Dervan et al., Science 251:1360 (1991)) or to the mRNA itself (antisense - Okano, J. Neurochem. 56:560 (1991); Oligodeoxy-nucleotides as Antisense Inhibitors of Gene Expression, CRC Press, Boca Raton, FL (1988).) Triple helix formation optimally results in a shut-off of RNA transcription from DNA, while antisense RNA hybridization blocks translation of an mRNA molecule into polypeptide. Both techniques are effective in model systems, and the information disclosed herein can be used to design antisense or triple helix polynucleotides in an effort to treat disease.

Polynucleotides of the present invention are also useful in gene therapy. One goal of gene therapy is to insert a normal gene into an organism having a defective gene, in an effort to correct the genetic defect. The polynucleotides disclosed in the present invention offer a means of targeting such genetic defects in a highly accurate manner. Another goal is to insert a new gene that was not present in the host genome, thereby producing a new trait in the host cell.

The polynucleotides are also useful for identifying individuals from minute biological samples. The United States military, for example, is considering the use of restriction fragment length polymorphism (RFLP) for identification of its personnel. In this technique, an individual's genomic DNA is digested with one or more restriction enzymes, and probed on a Southern blot to yield unique bands for identifying

personnel. This method does not suffer from the current limitations of "Dog Tags" which can be lost, switched, or stolen, making positive identification difficult. The polynucleotides of the present invention can be used as additional DNA markers for RFLP.

The polynucleotides of the present invention can also be used as an alternative to RFLP, by determining the actual base-by-base DNA sequence of selected portions of an individual's genome. These sequences can be used to prepare PCR primers for amplifying and isolating such selected DNA, which can then be sequenced. Using this technique, individuals can be identified because each individual will have a unique set of DNA sequences. Once an unique ID database is established for an individual, positive identification of that individual, living or dead, can be made from extremely small tissue samples.

Forensic biology also benefits from using DNA-based identification techniques as disclosed herein. DNA sequences taken from very small biological samples such as tissues, e.g., hair or skin, or body fluids, e.g., blood, saliva, semen, etc., can be amplified using PCR. In one prior art technique, gene sequences amplified from polymorphic loci, such as DQa class II HLA gene, are used in forensic biology to identify individuals. (Erlich, H., PCR Technology, Freeman and Co. (1992).) Once these specific polymorphic loci are amplified, they are digested with one or more restriction enzymes, yielding an identifying set of bands on a Southern blot probed with DNA corresponding to the DQa class II HLA gene. Similarly, polynucleotides of the present invention can be used as polymorphic markers for forensic purposes.

There is also a need for reagents capable of identifying the source of a particular tissue. Such need arises, for example, in forensics when presented with tissue of unknown origin. Appropriate reagents can comprise, for example, DNA probes or primers specific to particular tissue prepared from the sequences of the present invention. Panels of such reagents can identify tissue by species and/or by organ type. In a similar fashion, these reagents can be used to screen tissue cultures for contamination.

In the very least, the polynucleotides of the present invention can be used as molecular weight markers on Southern gels, as diagnostic probes for the presence of a specific mRNA in a particular cell type, as a probe to "subtract-out" known sequences in the process of discovering novel polynucleotides, for selecting and making oligomers for attachment to a "gene chip" or other support, to raise anti-DNA antibodies using DNA immunization techniques, and as an antigen to elicit an immune response.

Uses of the Polypeptides

Each of the polypeptides identified herein can be used in numerous ways. The following description should be considered exemplary and utilizes known techniques.

A polypeptide of the present invention can be used to assay protein levels in a biological sample using antibody-based techniques. For example, protein expression in tissues can be studied with classical immunohistological methods. (Jalkanen, M., et al., J. Cell. Biol. 101:976-985 (1985); Jalkanen, M., et al., J. Cell . Biol. 105:3087-3096 (1987).) Other antibody-based methods useful for detecting protein gene expression include immunoassays, such as the enzyme linked immunosorbent assay (ELISA) and the radioimmunoassay (RIA). Suitable antibody assay labels are known in the art and include enzyme labels, such as, glucose oxidase, and radioisotopes, such as iodine (125I, 121I), carbon (14C), sulfur (35S), tritium (3H), indium (112In), and technetium (99mTc), and fluorescent labels, such as fluorescein and rhodamine, and biotin.

In addition to assaying secreted protein levels in a biological sample, proteins can also be detected in vivo by imaging. Antibody labels or markers for in vivo imaging of protein include those detectable by X-radiography, NMR or ESR. For X-radiography, suitable labels include radioisotopes such as barium or cesium, which emit detectable radiation but are not overtly harmful to the subject. Suitable markers for NMR and ESR include those with a detectable characteristic spin, such as deuterium, which may be incorporated into the antibody by labeling of nutrients for the relevant hybridoma.

A protein-specific antibody or antibody fragment which has been labeled with an appropriate detectable imaging moiety, such as a radioisotope (for example, 131I, 112In, 99mTc), a radio-opaque substance, or a material detectable by nuclear magnetic resonance, is introduced (for example, parenterally, subcutaneously, or intraperitoneally) into the mammal. It will be understood in the art that the size of the subject and the imaging system used will determine the quantity of imaging moiety needed to produce diagnostic images. In the case of a radioisotope moiety, for a human subject, the quantity of radioactivity injected will normally range from about 5 to 20 millicuries of 99mTc. The labeled antibody or antibody fragment will then preferentially accumulate at the location of cells which contain the specific protein. In vivo tumor imaging is described in S.W. Burchiel et al., "Immunopharmacokinetics of Radiolabeled Antibodies and Their Fragments." (Chapter 13 in Tumor Imaging: The Radiochemical Detection of Cancer, S.W. Burchiel and B. A. Rhodes, eds., Masson Publishing Inc. (1982).)

Thus, the invention provides a diagnostic method of a disorder, which involves (a) assaying the expression of a polypeptide of the present invention in cells or body fluid of an individual; (b) comparing the level of gene expression with a standard gene expression level, whereby an increase or decrease in the assayed polypeptide gene expression level compared to the standard expression level is indicative of a disorder.

Moreover, polypeptides of the present invention can be used to treat disease. For example, patients can be administered a polypeptide of the present invention in an effort to replace absent or decreased levels of the polypeptide (e.g., insulin), to supplement absent or decreased levels of a different polypeptide (e.g., hemoglobin S for hemoglobin B), to inhibit the activity of a polypeptide (e.g., an oncogene), to activate the activity of a polypeptide (e.g., by binding to a receptor), to reduce the activity of a membrane bound receptor by competing with it for free ligand (e.g., soluble TNF receptors used in reducing inflammation), or to bring about a desired response (e.g., blood vessel growth).

Similarly, antibodies directed to a polypeptide of the present invention can also be used to treat disease. For example, administration of an antibody directed to a polypeptide of the present invention can bind and reduce overproduction of the polypeptide. Similarly, administration of an antibody can activate the polypeptide, such as by binding to a polypeptide bound to a membrane (receptor).

At the very least, the polypeptides of the present invention can be used as molecular weight markers on SDS-PAGE gels or on molecular sieve gel filtration columns using methods well known to those of skill in the art. Polypeptides can also be used to raise antibodies, which in turn are used to measure protein expression from a recombinant cell, as a way of assessing transformation of the host cell. Moreover, the polypeptides of the present invention can be used to test the following biological activities.

Biological Activities

The polynucleotides and polypeptides of the present invention can be used in assays to test for one or more biological activities. If these polynucleotides and polypeptides do exhibit activity in a particular assay, it is likely that these molecules may be involved in the diseases associated with the biological activity. Thus, the polynucleotides and polypeptides could be used to treat the associated disease.

Immune Activity

A polypeptide or polynucleotide of the present invention may be useful in treating deficiencies or disorders of the immune system, by activating or inhibiting the

proliferation, differentiation, or mobilization (chemotaxis) of immune cells. Immune cells develop through a process called hematopoiesis, producing myeloid (platelets, red blood cells, neutrophils, and macrophages) and lymphoid (B and T lymphocytes) cells from pluripotent stem cells. The etiology of these immune deficiencies or disorders may be genetic, somatic, such as cancer or some autoimmune disorders, acquired (e.g., by chemotherapy or toxins), or infectious. Moreover, a polynucleotide or polypeptide of the present invention can be used as a marker or detector of a particular immune system disease or disorder.

A polynucleotide or polypeptide of the present invention may be useful in treating or detecting deficiencies or disorders of hematopoietic cells. A polypeptide or polynucleotide of the present invention could be used to increase differentiation and proliferation of hematopoietic cells, including the pluripotent stem cells, in an effort to treat those disorders associated with a decrease in certain (or many) types hematopoietic cells. Examples of immunologic deficiency syndromes include, but are not limited to: blood protein disorders (e.g. agammaglobulinemia, dysgammaglobulinemia), ataxia telangiectasia, common variable immunodeficiency, Digeorge Syndrome, HIV infection, HTLV-BLV infection, leukocyte adhesion deficiency syndrome, lymphopenia, phagocyte bactericidal dysfunction, severe combined immunodeficiency (SCIDs), Wiskott-Aldrich Disorder, anemia, thrombocytopenia, or hemoglobinuria.

Moreover, a polypeptide or polynucleotide of the present invention could also be used to modulate hemostatic (the stopping of bleeding) or thrombolytic activity (clot formation). For example, by increasing hemostatic or thrombolytic activity, a polynucleotide or polypeptide of the present invention could be used to treat blood coagulation disorders (e.g., afibrinogenemia, factor deficiencies), blood platelet disorders (e.g. thrombocytopenia), or wounds resulting from trauma, surgery, or other causes. Alternatively, a polynucleotide or polypeptide of the present invention that can decrease hemostatic or thrombolytic activity could be used to inhibit or dissolve clotting. These molecules could be important in the treatment of heart attacks (infarction), strokes, or scarring.

A polynucleotide or polypeptide of the present invention may also be useful in treating or detecting autoimmune disorders. Many autoimmune disorders result from inappropriate recognition of self as foreign material by immune cells. This inappropriate recognition results in an immune response leading to the destruction of the host tissue. Therefore, the administration of a polypeptide or polynucleotide of the present invention that inhibits an immune response, particularly the proliferation, differentiation, or chemotaxis of T-cells, may be an effective therapy in preventing autoimmune disorders.

Examples of autoimmune disorders that can be treated or detected by the present invention include, but are not limited to: Addison's Disease, hemolytic anemia, antiphospholipid syndrome, rheumatoid arthritis, dermatitis, allergic encephalomyelitis, glomerulonephritis, Goodpasture's Syndrome, Graves' Disease, Multiple Sclerosis, Myasthenia Gravis, Neuritis, Ophthalmia, Bullous Pemphigoid, Pemphigus, Polyendocrinopathies, Purpura, Reiter's Disease, Stiff-Man Syndrome, Autoimmune Thyroiditis, Systemic Lupus Erythematosus, Autoimmune Pulmonary Inflammation, Guillain-Barre Syndrome, insulin dependent diabetes mellitis, and autoimmune inflammatory eye disease.

Similarly, allergic reactions and conditions, such as asthma (particularly allergic asthma) or other respiratory problems, may also be treated by a polypeptide or polynucleotide of the present invention. Moreover, these molecules can be used to treat anaphylaxis, hypersensitivity to an antigenic molecule, or blood group incompatibility.

A polynucleotide or polypeptide of the present invention may also be used to treat and/or prevent organ rejection or graft-versus-host disease (GVHD). Organ rejection occurs by host immune cell destruction of the transplanted tissue through an immune response. Similarly, an immune response is also involved in GVHD, but, in this case, the foreign transplanted immune cells destroy the host tissues. The administration of a polypeptide or polynucleotide of the present invention that inhibits an immune response, particularly the proliferation, differentiation, or chemotaxis of T-cells, may be an effective therapy in preventing organ rejection or GVHD.

Similarly, a polypeptide or polynucleotide of the present invention may also be used to modulate inflammation. For example, the polypeptide or polynucleotide may inhibit the proliferation and differentiation of cells involved in an inflammatory response. These molecules can be used to treat inflammatory conditions, both chronic and acute conditions, including inflammation associated with infection (e.g., septic shock, sepsis, or systemic inflammatory response syndrome (SIRS)), ischemia-reperfusion injury, endotoxin lethality, arthritis, complement-mediated hyperacute rejection, nephritis, cytokine or chemokine induced lung injury, inflammatory bowel disease, Crohn's disease, or resulting from over production of cytokines (e.g., TNF or IL-1.)

Hyperproliferative Disorders

A polypeptide or polynucleotide can be used to treat or detect hyperproliferative disorders, including neoplasms. A polypeptide or polynucleotide of the present invention may inhibit the proliferation of the disorder through direct or indirect

interactions. Alternatively, a polypeptide or polynucleotide of the present invention may proliferate other cells which can inhibit the hyperproliferative disorder.

For example, by increasing an immune response, particularly increasing antigenic qualities of the hyperproliferative disorder or by proliferating, differentiating, or mobilizing T-cells, hyperproliferative disorders can be treated. This immune response may be increased by either enhancing an existing immune response, or by initiating a new immune response. Alternatively, decreasing an immune response may also be a method of treating hyperproliferative disorders, such as a chemotherapeutic agent.

Examples of hyperproliferative disorders that can be treated or detected by a polynucleotide or polypeptide of the present invention include, but are not limited to neoplasms located in the: abdomen, bone, breast, digestive system, liver, pancreas, peritoneum, endocrine glands (adrenal, parathyroid, pituitary, testicles, ovary, thymus, thyroid), eye, head and neck, nervous (central and peripheral), lymphatic system, pelvic, skin, soft tissue, spleen, thoracic, and urogenital.

Similarly, other hyperproliferative disorders can also be treated or detected by a polynucleotide or polypeptide of the present invention. Examples of such hyperproliferative disorders include, but are not limited to: hypergammaglobulinemia, lymphoproliferative disorders, paraproteinemias, purpura, sarcoidosis, Sezary Syndrome, Waldenstron's Macroglobulinemia, Gaucher's Disease, histiocytosis, and any other hyperproliferative disease, besides neoplasia, located in an organ system listed above.

Infectious Disease

A polypeptide or polynucleotide of the present invention can be used to treat or detect infectious agents. For example, by increasing the immune response, particularly increasing the proliferation and differentiation of B and/or T cells, infectious diseases may be treated. The immune response may be increased by either enhancing an existing immune response, or by initiating a new immune response. Alternatively, the polypeptide or polynucleotide of the present invention may also directly inhibit the infectious agent, without necessarily eliciting an immune response.

Viruses are one example of an infectious agent that can cause disease or symptoms that can be treated or detected by a polynucleotide or polypeptide of the present invention. Examples of viruses, include, but are not limited to the following DNA and RNA viral families: Arbovirus, Adenoviridae, Arenaviridae, Arterivirus, Birnaviridae, Bunyaviridae, Caliciviridae, Circoviridae, Coronaviridae, Flaviviridae, Hepadnaviridae (Hepatitis), Herpesviridae (such as, Cytomegalovirus, Herpes

Simplex, Herpes Zoster), Mononegavirus (e.g., Paramyxoviridae, Morbillivirus, Rhabdoviridae), Orthomyxoviridae (e.g., Influenza), Papovaviridae, Parvoviridae, Picornaviridae, Poxviridae (such as Smallpox or Vaccinia), Reoviridae (e.g., Rotavirus), Retroviridae (HTLV-I, HTLV-II, Lentivirus), and Togaviridae (e.g., Rubivirus). Viruses falling within these families can cause a variety of diseases or symptoms, including, but not limited to: arthritis, bronchiollitis, encephalitis, eye infections (e.g., conjunctivitis, keratitis), chronic fatigue syndrome, hepatitis (A, B, C, E, Chronic Active, Delta), meningitis, opportunistic infections (e.g., AIDS), pneumonia, Burkitt's Lymphoma, chickenpox , hemorrhagic fever, Measles, Mumps, Parainfluenza, Rabies, the common cold, Polio, leukemia, Rubella, sexually transmitted diseases, skin diseases (e.g., Kaposi's, warts), and viremia. A polypeptide or polynucleotide of the present invention can be used to treat or detect any of these symptoms or diseases.

Similarly, bacterial or fungal agents that can cause disease or symptoms and that can be treated or detected by a polynucleotide or polypeptide of the present invention include, but not limited to, the following Gram-Negative and Gram-positive bacterial families and fungi: Actinomycetales (e.g., Corynebacterium, Mycobacterium, Norcardia), Aspergillosis, Bacillaceae (e.g., Anthrax, Clostridium), Bacteroidaceae, Blastomycosis, Bordetella, Borrelia, Brucellosis, Candidiasis, Campylobacter, Coccidioidomycosis, Cryptococcosis, Dermatocycoses, Enterobacteriaceae (Klebsiella, Salmonella, Serratia, Yersinia), Erysipelothrix, Helicobacter, Legionellosis, Leptospirosis, Listeria, Mycoplasmatales, Neisseriaceae (e.g., Acinetobacter, Gonorrhea, Menigococcal), Pasteurellacea Infections (e.g., Actinobacillus, Heamophilus, Pasteurella), Pseudomonas, Rickettsiaceae, Chlamydiaceae, Syphilis, and Staphylococcal. These bacterial or fungal families can cause the following diseases or symptoms. including, but not limited to: bacteremia, endocarditis, eye infections (conjunctivitis, tuberculosis, uveitis), gingivitis, opportunistic infections (e.g., AIDS related infections), paronychia, prosthesis-related infections, Reiter's Disease, respiratory tract infections, such as Whooping Cough or Empyema, sepsis, Lyme Disease, Cat-Scratch Disease, Dysentery, Paratyphoid Fever, food poisoning, Typhoid, pneumonia, Gonorrhea, meningitis, Chlamydia, Syphilis, Diphtheria, Leprosy, Paratuberculosis, Tuberculosis, Lupus, Botulism, gangrene, tetanus, impetigo, Rheumatic Fever, Scarlet Fever, sexually transmitted diseases, skin diseases (e.g., cellulitis, dermatocycoses), toxemia, urinary tract infections, wound infections. A polypeptide or polynucleotide of the present invention can be used to treat or detect any of these symptoms or diseases.

Moreover, parasitic agents causing disease or symptoms that can be treated or detected by a polynucleotide or polypeptide of the present invention include, but not limited to, the following families: Amebiasis, Babesiosis, Coccidiosis, Cryptosporidiosis, Dientamoebiasis, Dourine, Ectoparasitic, Giardiasis, Helminthiasis, Leishmaniasis, Theileriasis, Toxoplasmosis, Trypanosomiasis, and Trichomonas. These parasites can cause a variety of diseases or symptoms, including, but not limited to: Scabies, Trombiculiasis, eye infections, intestinal disease (e.g., dysentery, giardiasis), liver disease, lung disease, opportunistic infections (e.g., AIDS related), Malaria, pregnancy complications, and toxoplasmosis. A polypeptide or polynucleotide of the present invention can be used to treat or detect any of these symptoms or diseases.

Preferably, treatment using a polypeptide or polynucleotide of the present invention could either be by administering an effective amount of a polypeptide to the patient, or by removing cells from the patient, supplying the cells with a polynucleotide of the present invention, and returning the engineered cells to the patient (ex vivo therapy). Moreover, the polypeptide or polynucleotide of the present invention can be used as an antigen in a vaccine to raise an immune response against infectious disease.

Regeneration

A polynucleotide or polypeptide of the present invention can be used to differentiate, proliferate, and attract cells, leading to the regeneration of tissues. (See, Science 276:59-87 (1997).) The regeneration of tissues could be used to repair, replace, or protect tissue damaged by congenital defects, trauma (wounds, burns, incisions, or ulcers), age, disease (e.g. osteoporosis, osteocarthritis, periodontal disease, liver failure), surgery, including cosmetic plastic surgery, fibrosis, reperfusion injury, or systemic cytokine damage.

Tissues that could be regenerated using the present invention include organs (e.g., pancreas, liver, intestine, kidney, skin, endothelium), muscle (smooth, skeletal or cardiac), vascular (including vascular endothelium), nervous, hematopoietic, and skeletal (bone, cartilage, tendon, and ligament) tissue. Preferably, regeneration occurs without or decreased scarring. Regeneration also may include angiogenesis.

Moreover, a polynucleotide or polypeptide of the present invention may increase regeneration of tissues difficult to heal. For example, increased tendon/ligament regeneration would quicken recovery time after damage. A polynucleotide or polypeptide of the present invention could also be used prophylactically in an effort to avoid damage. Specific diseases that could be treated include of tendinitis, carpal tunnel syndrome, and other tehdon or ligament defects. A further example of tissue

regeneration of non-healing wounds includes pressure ulcers, ulcers associated with vascular insufficiency, surgical, and traumatic wounds.

Similarly, nerve and brain tissue could also be regenerated by using a polynucleotide or polypeptide of the present invention to proliferate and differentiate nerve cells. Diseases that could be treated using this method include central and peripheral nervous system diseases, neuropathies, or mechanical and traumatic disorders (e.g., spinal cord disorders, head trauma, cerebrovascular disease, and stoke). Specifically, diseases associated with peripheral nerve injuries, peripheral neuropathy (e.g., resulting from chemotherapy or other medical therapies), localized neuropathies, and central nervous system diseases (e.g., Alzheimer's disease, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and Shy-Drager syndrome), could all be treated using the polynucleotide or polypeptide of the present invention.

Chemotaxis

A polynucleotide or polypeptide of the present invention may have chemotaxis activity. A chemotaxic molecule attracts or mobilizes cells (e.g., monocytes, fibroblasts, neutrophils, T-cells, mast cells, eosinophils, epithelial and/or endothelial cells) to a particular site in the body, such as inflammation, infection, or site of hyperproliferation. The mobilized cells can then fight off and/or heal the particular trauma or abnormality.

A polynucleotide or polypeptide of the present invention may increase chemotaxic activity of particular cells. These chemotactic molecules can then be used to treat inflammation, infection, hyperproliferative disorders, or any immune system disorder by increasing the number of cells targeted to a particular location in the body. For example, chemotaxic molecules can be used to treat wounds and other trauma to tissues by attracting immune cells to the injured location. Chemotactic molecules of the present invention can also attract fibroblasts, which can be used to treat wounds.

It is also contemplated that a polynucleotide or polypeptide of the present invention may inhibit chemotactic activity. These molecules could also be used to treat disorders. Thus, a polynucleotide or polypeptide of the present invention could be used as an inhibitor of chemotaxis.

Binding Activity

A polypeptide of the present invention may be used to screen for molecules that bind to the polypeptide or for molecules to which the polypeptide binds. The binding of the polypeptide and the molecule may activate (agonist), increase, inhibit

(antagonist), or decrease activity of the polypeptide or the molecule bound. Examples of such molecules include antibodies, oligonucleotides, proteins (e.g., receptors),or small molecules.

Preferably, the molecule is closely related to the natural ligand of the polypeptide, e.g., a fragment of the ligand, or a natural substrate, a ligand, a structural or functional mimetic. (See, Coligan et al., Current Protocols in Immunology 1(2):Chapter 5 (1991).) Similarly, the molecule can be closely related to the natural receptor to which the polypeptide binds, or at least, a fragment of the receptor capable of being bound by the polypeptide (e.g., active site). In either case, the molecule can be rationally designed using known techniques.

Preferably, the screening for these molecules involves producing appropriate cells which express the polypeptide, either as a secreted protein or on the cell membrane. Preferred cells include cells from mammals, yeast, Drosophila, or *E. coli*. Cells expressing the polypeptide (or cell membrane containing the expressed polypeptide) are then preferably contacted with a test compound potentially containing the molecule to observe binding, stimulation, or inhibition of activity of either the polypeptide or the molecule.

The assay may simply test binding of a candidate compound to the polypeptide, wherein binding is detected by a label, or in an assay involving competition with a labeled competitor. Further, the assay may test whether the candidate compound results in a signal generated by binding to the polypeptide.

Alternatively, the assay can be carried out using cell-free preparations, polypeptide/molecule affixed to a solid support, chemical libraries, or natural product mixtures. The assay may also simply comprise the steps of mixing a candidate compound with a solution containing a polypeptide, measuring polypeptide/molecule activity or binding, and comparing the polypeptide/molecule activity or binding to a standard.

Preferably, an ELISA assay can measure polypeptide level or activity in a sample (e.g., biological sample) using a monoclonal or polyclonal antibody. The antibody can measure polypeptide level or activity by either binding, directly or indirectly, to the polypeptide or by competing with the polypeptide for a substrate.

All of these above assays can be used as diagnostic or prognostic markers. The molecules discovered using these assays can be used to treat disease or to bring about a particular result in a patient (e.g., blood vessel growth) by activating or inhibiting the polypeptide/molecule. Moreover, the assays can discover agents which may inhibit or enhance the production of the polypeptide from suitably manipulated cells or tissues.

Therefore, the invention includes a method of identifying compounds which bind to a polypeptide of the invention comprising the steps of: (a) incubating a candidate binding compound with a polypeptide of the invention; and (b) determining if binding has occurred. Moreover, the invention includes a method of identifying agonists/antagonists comprising the steps of: (a) incubating a candidate compound with a polypeptide of the invention, (b) assaying a biological activity , and (b) determining if a biological activity of the polypeptide has been altered.

Other Activities

A polypeptide or polynucleotide of the present invention may also increase or decrease the differentiation or proliferation of embryonic stem cells, besides, as discussed above, hematopoietic lineage.

A polypeptide or polynucleotide of the present invention may also be used to modulate mammalian characteristics, such as body height, weight, hair color, eye color, skin, percentage of adipose tissue, pigmentation, size, and shape (e.g., cosmetic surgery). Similarly, a polypeptide or polynucleotide of the present invention may be used to modulate mammalian metabolism affecting catabolism, anabolism, processing, utilization, and storage of energy.

A polypeptide or polynucleotide of the present invention may be used to change a mammal's mental state or physical state by influencing biorhythms, caricadic rhythms, depression (including depressive disorders), tendency for violence, tolerance for pain, reproductive capabilities (preferably by Activin or Inhibin-like activity), hormonal or endocrine levels, appetite, libido, memory, stress, or other cognitive qualities.

A polypeptide or polynucleotide of the present invention may also be used as a food additive or preservative, such as to increase or decrease storage capabilities, fat content, lipid, protein, carbohydrate, vitamins, minerals, cofactors or other nutritional components.

Other Preferred Embodiments

Other preferred embodiments of the claimed invention include an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least about 50 contiguous nucleotides in the nucleotide sequence of SEQ ID NO:X wherein X is any integer as defined in Table 1.

Also preferred is a nucleic acid molecule wherein said sequence of contiguous nucleotides is included in the nucleotide sequence of SEQ ID NO:X in the range of

positions beginning with the nucleotide at about the position of the 5' Nucleotide of the Clone Sequence and ending with the nucleotide at about the position of the 3' Nucleotide of the Clone Sequence as defined for SEQ ID NO:X in Table 1.

Also preferred is a nucleic acid molecule wherein said sequence of contiguous nucleotides is included in the nucleotide sequence of SEQ ID NO:X in the range of positions beginning with the nucleotide at about the position of the 5' Nucleotide of the Start Codon and ending with the nucleotide at about the position of the 3' Nucleotide of the Clone Sequence as defined for SEQ ID NO:X in Table 1.

Similarly preferred is a nucleic acid molecule wherein said sequence of contiguous nucleotides is included in the nucleotide sequence of SEQ ID NO:X in the range of positions beginning with the nucleotide at about the position of the 5' Nucleotide of the First Amino Acid of the Signal Peptide and ending with the nucleotide at about the position of the 3' Nucleotide of the Clone Sequence as defined for SEQ ID NO:X in Table 1.

Also preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least about 150 contiguous nucleotides in the nucleotide sequence of SEQ ID NO:X.

Further preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least about 500 contiguous nucleotides in the nucleotide sequence of SEQ ID NO:X.

A further preferred embodiment is a nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to the nucleotide sequence of SEQ ID NO:X beginning with the nucleotide at about the position of the 5' Nucleotide of the First Amino Acid of the Signal Peptide and ending with the nucleotide at about the position of the 3' Nucleotide of the Clone Sequence as defined for SEQ ID NO:X in Table 1.

A further preferred embodiment is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to the complete nucleotide sequence of SEQ ID NO:X.

Also preferred is an isolated nucleic acid molecule which hybridizes under stringent hybridization conditions to a nucleic acid molecule, wherein said nucleic acid molecule which hybridizes does not hybridize under stringent hybridization conditions to a nucleic acid molecule having a nucleotide sequence consisting of only A residues or of only T residues.

Also preferred is a composition of matter comprising a DNA molecule which comprises a human cDNA clone identified by a cDNA Clone Identifier in Table 1, which DNA molecule is contained in the material deposited with the American Type

Culture Collection and given the ATCC Deposit Number shown in Table 1 for said cDNA Clone Identifier.

Also preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least 50 contiguous nucleotides in the nucleotide sequence of a human cDNA clone identified by a cDNA Clone Identifier in Table 1, which DNA molecule is contained in the deposit given the ATCC Deposit Number shown in Table 1.

Also preferred is an isolated nucleic acid molecule, wherein said sequence of at least 50 contiguous nucleotides is included in the nucleotide sequence of the complete open reading frame sequence encoded by said human cDNA clone.

Also preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to sequence of at least 150 contiguous nucleotides in the nucleotide sequence encoded by said human cDNA clone.

A further preferred embodiment is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to sequence of at least 500 contiguous nucleotides in the nucleotide sequence encoded by said human cDNA clone.

A further preferred embodiment is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to the complete nucleotide sequence encoded by said human cDNA clone.

A further preferred embodiment is a method for detecting in a biological sample a nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from the group consisting of: a nucleotide sequence of SEQ ID NO:X wherein X is any integer as defined in Table 1; and a nucleotide sequence encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1; which method comprises a step of comparing a nucleotide sequence of at least one nucleic acid molecule in said sample with a sequence selected from said group and determining whether the sequence of said nucleic acid molecule in said sample is at least 95% identical to said selected sequence.

Also preferred is the above method wherein said step of comparing sequences comprises determining the extent of nucleic acid hybridization between nucleic acid molecules in said sample and a nucleic acid molecule comprising said sequence selected from said group. Similarly, also preferred is the above method wherein said step of comparing sequences is performed by comparing the nucleotide sequence determined from a nucleic acid molecule in said sample with said sequence selected from said group. The nucleic acid molecules can comprise DNA molecules or RNA molecules.

A further preferred embodiment is a method for identifying the species, tissue or cell type of a biological sample which method comprises a step of detecting nucleic acid molecules in said sample, if any, comprising a nucleotide sequence that is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from the group consisting of: a nucleotide sequence of SEQ ID NO:X wherein X is any integer as defined in Table 1; and a nucleotide sequence encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

The method for identifying the species, tissue or cell type of a biological sample can comprise a step of detecting nucleic acid molecules comprising a nucleotide sequence in a panel of at least two nucleotide sequences, wherein at least one sequence in said panel is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from said group.

Also preferred is a method for diagnosing in a subject a pathological condition associated with abnormal structure or expression of a gene encoding a secreted protein identified in Table 1, which method comprises a step of detecting in a biological sample obtained from said subject nucleic acid molecules, if any, comprising a nucleotide sequence that is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from the group consisting of: a nucleotide sequence of SEQ ID NO:X wherein X is any integer as defined in Table 1; and a nucleotide sequence encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

The method for diagnosing a pathological condition can comprise a step of detecting nucleic acid molecules comprising a nucleotide sequence in a panel of at least two nucleotide sequences, wherein at least one sequence in said panel is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from said group.

Also preferred is a composition of matter comprising isolated nucleic acid molecules wherein the nucleotide sequences of said nucleic acid molecules comprise a panel of at least two nucleotide sequences, wherein at least one sequence in said panel is at least 95% identical to a sequence of at least 50 contiguous nucleotides in a sequence selected from the group consisting of: a nucleotide sequence of SEQ ID NO:X wherein X is any integer as defined in Table 1; and a nucleotide sequence encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1. The nucleic acid molecules can comprise DNA molecules or RNA molecules.

Also preferred is an isolated polypeptide comprising an amino acid sequence at least 90% identical to a sequence of at least about 10 contiguous amino acids in the amino acid sequence of SEQ ID NO:Y wherein Y is any integer as defined in Table 1.

Also preferred is a polypeptide, wherein said sequence of contiguous amino acids is included in the amino acid sequence of SEQ ID NO:Y in the range of positions beginning with the residue at about the position of the First Amino Acid of the Secreted Portion and ending with the residue at about the Last Amino Acid of the Open Reading Frame as set forth for SEQ ID NO:Y in Table 1.

Also preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence of at least about 30 contiguous amino acids in the amino acid sequence of SEQ ID NO:Y.

Further preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence of at least about 100 contiguous amino acids in the amino acid sequence of SEQ ID NO:Y.

Further preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to the complete amino acid sequence of SEQ ID NO:Y.

Further preferred is an isolated polypeptide comprising an amino acid sequence at least 90% identical to a sequence of at least about 10 contiguous amino acids in the complete amino acid sequence of a secreted protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Also preferred is a polypeptide wherein said sequence of contiguous amino acids is included in the amino acid sequence of a secreted portion of the secreted protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Also preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence of at least about 30 contiguous amino acids in the amino acid sequence of the secreted portion of the protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Also preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence of at least about 100 contiguous amino acids in the amino acid sequence of the secreted portion of the protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Also preferred is an isolated polypeptide comprising an amino acid sequence at least 95% identical to the amino acid sequence of the secreted portion of the protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Further preferred is an isolated antibody which binds specifically to a polypeptide comprising an amino acid sequence that is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: an amino acid sequence of SEQ ID NO:Y wherein Y is any integer as defined in Table 1; and a complete amino acid sequence of a protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Further preferred is a method for detecting in a biological sample a polypeptide comprising an amino acid sequence which is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: an amino acid sequence of SEQ ID NO:Y wherein Y is any integer as defined in Table 1; and a complete amino acid sequence of a protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1; which method comprises a step of comparing an amino acid sequence of at least one polypeptide molecule in said sample with a sequence selected from said group and determining whether the sequence of said polypeptide molecule in said sample is at least 90% identical to said sequence of at least 10 contiguous amino acids.

Also preferred is the above method wherein said step of comparing an amino acid sequence of at least one polypeptide molecule in said sample with a sequence selected from said group comprises determining the extent of specific binding of polypeptides in said sample to an antibody which binds specifically to a polypeptide comprising an amino acid sequence that is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: an amino acid sequence of SEQ ID NO:Y wherein Y is any integer as defined in Table 1; and a complete amino acid sequence of a protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Also preferred is the above method wherein said step of comparing sequences is performed by comparing the amino acid sequence determined from a polypeptide molecule in said sample with said sequence selected from said group.

Also preferred is a method for identifying the species, tissue or cell type of a biological sample which method comprises a step of detecting polypeptide molecules in said sample, if any, comprising an amino acid sequence that is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: an amino acid sequence of SEQ ID NO:Y wherein Y is any integer as defined in Table 1; and a complete amino acid sequence of a secreted protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Also preferred is the above method for identifying the species, tissue or cell type of a biological sample, which method comprises a step of detecting polypeptide molecules comprising an amino acid sequence in a panel of at least two amino acid sequences, wherein at least one sequence in said panel is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the above group.

Also preferred is a method for diagnosing in a subject a pathological condition associated with abnormal structure or expression of a gene encoding a secreted protein identified in Table 1, which method comprises a step of detecting in a biological sample obtained from said subject polypeptide molecules comprising an amino acid sequence in a panel of at least two amino acid sequences, wherein at least one sequence in said panel is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: an amino acid sequence of SEQ ID NO:Y wherein Y is any integer as defined in Table 1; and a complete amino acid sequence of a secreted protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

In any of these methods, the step of detecting said polypeptide molecules includes using an antibody.

Also preferred is an isolated nucleic acid molecule comprising a nucleotide sequence which is at least 95% identical to a nucleotide sequence encoding a polypeptide wherein said polypeptide comprises an amino acid sequence that is at least 90% identical to a sequence of at least 10 contiguous amino acids in a sequence selected from the group consisting of: an amino acid sequence of SEQ ID NO:Y wherein Y is any integer as defined in Table 1; and a complete amino acid sequence of a secreted protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Also preferred is an isolated nucleic acid molecule, wherein said nucleotide sequence encoding a polypeptide has been optimized for expression of said polypeptide in a prokaryotic host.

Also preferred is an isolated nucleic acid molecule, wherein said polypeptide comprises an amino acid sequence selected from the group consisting of: an amino acid sequence of SEQ ID NO:Y wherein Y is any integer as defined in Table 1; and a complete amino acid sequence of a secreted protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1.

Further preferred is a method of making a recombinant vector comprising inserting any of the above isolated nucleic acid molecule into a vector. Also preferred is the recombinant vector produced by this method. Also preferred is a method of making a recombinant host cell comprising introducing the vector into a host cell, as well as the recombinant host cell produced by this method.

Also preferred is a method of making an isolated polypeptide comprising culturing this recombinant host cell under conditions such that said polypeptide is expressed and recovering said polypeptide. Also preferred is this method of making an isolated polypeptide, wherein said recombinant host cell is a eukaryotic cell and said polypeptide is a secreted portion of a human secreted protein comprising an amino acid sequence selected from the group consisting of: an amino acid sequence of SEQ ID NO:Y beginning with the residue at the position of the First Amino Acid of the Secreted Portion of SEQ ID NO:Y wherein Y is an integer set forth in Table 1 and said position of the First Amino Acid of the Secreted Portion of SEQ ID NO:Y is defined in Table 1; and an amino acid sequence of a secreted portion of a protein encoded by a human cDNA clone identified by a cDNA Clone Identifier in Table 1 and contained in the deposit with the ATCC Deposit Number shown for said cDNA clone in Table 1. The isolated polypeptide produced by this method is also preferred.

Also preferred is a method of treatment of an individual in need of an increased level of a secreted protein activity, which method comprises administering to such an individual a pharmaceutical composition comprising an amount of an isolated polypeptide, polynucleotide, or antibody of the claimed invention effective to increase the level of said protein activity in said individual.

Having generally described the invention, the same will be more readily understood by reference to the following examples, which are provided by way of illustration and are not intended as limiting.

Examples

Example 1: Isolation of a Selected cDNA Clone From the Deposited Sample

Each cDNA clone in a cited ATCC deposit is contained in a plasmid vector. Table 1 identifies the vectors used to construct the cDNA library from which each clone was isolated. In many cases, the vector used to construct the library is a phage vector from which a plasmid has been excised. The table immediately below correlates the related plasmid for each phage vector used in constructing the cDNA library. For example, where a particular clone is identified in Table 1 as being isolated in the vector "Lambda Zap," the corresponding deposited clone is in "pBluescript."

Vector Used to Construct Library	Corresponding Deposited Plasmid
Lambda Zap	pBluescript (pBS)
Uni-Zap XR	pBluescript (pBS)
Zap Express	pBK
lafmid BA	plafmid BA
pSport1	pSport1
pCMVSport 2.0	pCMVSport 2.0
pCMVSport 3.0	pCMVSport 3.0
pCR®2.1	pCR®2.1

Vectors Lambda Zap (U.S. Patent Nos. 5,128,256 and 5,286,636), Uni-Zap XR (U.S. Patent Nos. 5,128, 256 and 5,286,636), Zap Express (U.S. Patent Nos. 5,128,256 and 5,286,636), pBluescript (pBS) (Short, J. M. et al., Nucleic Acids Res. 16:7583-7600 (1988); Alting-Mees, M. A. and Short, J. M., Nucleic Acids Res. 17:9494 (1989)) and pBK (Alting-Mees, M. A. et al., Strategies 5:58-61 (1992)) are commercially available from Stratagene Cloning Systems, Inc., 11011 N. Torrey Pines Road, La Jolla, CA, 92037. pBS contains an ampicillin resistance gene and pBK contains a neomycin resistance gene. Both can be transformed into E. coli strain XL-1 Blue, also available from Stratagene. pBS comes in 4 forms SK+, SK-, KS+ and KS. The S and K refers to the orientation of the polylinker to the T7 and T3 primer sequences which flank the polylinker region ("S" is for SacI and "K" is for KpnI which are the first sites on each respective end of the linker). "+" or "-" refer to the orientation of the f1 origin of replication ("ori"), such that in one orientation, single stranded rescue initiated from the f1 ori generates sense strand DNA and in the other, antisense.

Vectors pSport1, pCMVSport 2.0 and pCMVSport 3.0, were obtained from Life Technologies, Inc., P. O. Box 6009, Gaithersburg, MD 20897. All Sport vectors contain an ampicillin resistance gene and may be transformed into E. coli strain

DH10B, also available from Life Technologies. (See, for instance, Gruber, C. E., et al., Focus 15:59 (1993).) Vector lafmid BA (Bento Soares, Columbia University, NY) contains an ampicillin resistance gene and can be transformed into E. coli strain XL-1 Blue. Vector pCR®2.1, which is available from Invitrogen, 1600 Faraday Avenue, Carlsbad, CA 92008, contains an ampicillin resistance gene and may be transformed into E. coli strain DH10B, available from Life Technologies. (See, for instance, Clark, J. M., Nuc. Acids Res. 16:9677-9686 (1988) and Mead, D. et al., Bio/Technology 9: (1991).) Preferably, a polynucleotide of the present invention does not comprise the phage vector sequences identified for the particular clone in Table 1, as well as the corresponding plasmid vector sequences designated above.

The deposited material in the sample assigned the ATCC Deposit Number cited in Table 1 for any given cDNA clone also may contain one or more additional plasmids, each comprising a cDNA clone different from that given clone. Thus, deposits sharing the same ATCC Deposit Number contain at least a plasmid for each cDNA clone identified in Table 1. Typically, each ATCC deposit sample cited in Table 1 comprises a mixture of approximately equal amounts (by weight) of about 50 plasmid DNAs, each containing a different cDNA clone; but such a deposit sample may include plasmids for more or less than 50 cDNA clones, up to about 500 cDNA clones.

Two approaches can be used to isolate a particular clone from the deposited sample of plasmid DNAs cited for that clone in Table 1. First, a plasmid is directly isolated by screening the clones using a polynucleotide probe corresponding to SEQ ID NO:X.

Particularly, a specific polynucleotide with 30-40 nucleotides is synthesized using an Applied Biosystems DNA synthesizer according to the sequence reported. The oligonucleotide is labeled, for instance, with ^{32}P-γ-ATP using T4 polynucleotide kinase and purified according to routine methods. (E.g., Maniatis et al., Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Press, Cold Spring, NY (1982).) The plasmid mixture is transformed into a suitable host, as indicated above (such as XL-1 Blue (Stratagene)) using techniques known to those of skill in the art, such as those provided by the vector supplier or in related publications or patents cited above. The transformants are plated on 1.5% agar plates (containing the appropriate selection agent, e.g., ampicillin) to a density of about 150 transformants (colonies) per plate. These plates are screened using Nylon membranes according to routine methods for bacterial colony screening (e.g., Sambrook et al., Molecular Cloning: A Laboratory Manual, 2nd Edit., (1989), Cold Spring Harbor Laboratory Press, pages 1.93 to 1.104), or other techniques known to those of skill in the art.

Alternatively, two primers of 17-20 nucleotides derived from both ends of the SEQ ID NO:X (i.e., within the region of SEQ ID NO:X bounded by the 5' NT and the 3' NT of the clone defined in Table 1) are synthesized and used to amplify the desired cDNA using the deposited cDNA plasmid as a template. The polymerase chain reaction is carried out under routine conditions, for instance, in 25 µl of reaction mixture with 0.5 ug of the above cDNA template. A convenient reaction mixture is 1.5-5 mM $MgCl_2$, 0.01% (w/v) gelatin, 20 µM each of dATP, dCTP, dGTP, dTTP, 25 pmol of each primer and 0.25 Unit of Taq polymerase. Thirty five cycles of PCR (denaturation at 94°C for 1 min; annealing at 55°C for 1 min; elongation at 72°C for 1 min) are performed with a Perkin-Elmer Cetus automated thermal cycler. The amplified product is analyzed by agarose gel electrophoresis and the DNA band with expected molecular weight is excised and purified. The PCR product is verified to be the selected sequence by subcloning and sequencing the DNA product.

Several methods are available for the identification of the 5' or 3' non-coding portions of a gene which may not be present in the deposited clone. These methods include but are not limited to, filter probing, clone enrichment using specific probes, and protocols similar or identical to 5' and 3' "RACE" protocols which are well known in the art. For instance, a method similar to 5' RACE is available for generating the missing 5' end of a desired full-length transcript. (Fromont-Racine et al., Nucleic Acids Res. 21(7):1683-1684 (1993).)

Briefly, a specific RNA oligonucleotide is ligated to the 5' ends of a population of RNA presumably containing full-length gene RNA transcripts. A primer set containing a primer specific to the ligated RNA oligonucleotide and a primer specific to a known sequence of the gene of interest is used to PCR amplify the 5' portion of the desired full-length gene. This amplified product may then be sequenced and used to generate the full length gene.

This above method starts with total RNA isolated from the desired source, although poly-A+ RNA can be used. The RNA preparation can then be treated with phosphatase if necessary to eliminate 5' phosphate groups on degraded or damaged RNA which may interfere with the later RNA ligase step. The phosphatase should then be inactivated and the RNA treated with tobacco acid pyrophosphatase in order to remove the cap structure present at the 5' ends of messenger RNAs. This reaction leaves a 5' phosphate group at the 5' end of the cap cleaved RNA which can then be ligated to an RNA oligonucleotide using T4 RNA ligase.

This modified RNA preparation is used as a template for first strand cDNA synthesis using a gene specific oligonucleotide. The first strand synthesis reaction is

used as a template for PCR amplification of the desired 5' end using a primer specific to the ligated RNA oligonucleotide and a primer specific to the known sequence of the gene of interest. The resultant product is then sequenced and analyzed to confirm that the 5' end sequence belongs to the desired gene.

Example 2: Isolation of Genomic Clones Corresponding to a Polynucleotide

A human genomic P1 library (Genomic Systems, Inc.) is screened by PCR using primers selected for the cDNA sequence corresponding to SEQ ID NO:X., according to the method described in Example 1. (See also, Sambrook.)

Example 3: Tissue Distribution of Polypeptide

Tissue distribution of mRNA expression of polynucleotides of the present invention is determined using protocols for Northern blot analysis, described by, among others, Sambrook et al. For example, a cDNA probe produced by the method described in Example 1 is labeled with P^{32} using the rediprime™ DNA labeling system (Amersham Life Science), according to manufacturer's instructions. After labeling, the probe is purified using CHROMA SPIN-100™ column (Clontech Laboratories, Inc.), according to manufacturer's protocol number PT1200-1. The purified labeled probe is then used to examine various human tissues for mRNA expression.

Multiple Tissue Northern (MTN) blots containing various human tissues (H) or human immune system tissues (IM) (Clontech) are examined with the labeled probe using ExpressHyb™ hybridization solution (Clontech) according to manufacturer's protocol number PT1190-1. Following hybridization and washing, the blots are mounted and exposed to film at -70°C overnight, and the films developed according to standard procedures.

Example 4: Chromosomal Mapping of the Polynucleotides

An oligonucleotide primer set is designed according to the sequence at the 5' end of SEQ ID NO:X. This primer preferably spans about 100 nucleotides. This primer set is then used in a polymerase chain reaction under the following set of conditions : 30 seconds, 95°C; 1 minute, 56°C; 1 minute, 70°C. This cycle is repeated 32 times followed by one 5 minute cycle at 70°C. Human, mouse, and hamster DNA is used as template in addition to a somatic cell hybrid panel containing individual chromosomes or chromosome fragments (Bios, Inc). The reactions is analyzed on

either 8% polyacrylamide gels or 3.5 % agarose gels. Chromosome mapping is determined by the presence of an approximately 100 bp PCR fragment in the particular somatic cell hybrid.

Example 5: Bacterial Expression of a Polypeptide

A polynucleotide encoding a polypeptide of the present invention is amplified using PCR oligonucleotide primers corresponding to the 5' and 3' ends of the DNA sequence, as outlined in Example 1, to synthesize insertion fragments. The primers used to amplify the cDNA insert should preferably contain restriction sites, such as BamHI and XbaI, at the 5' end of the primers in order to clone the amplified product into the expression vector. For example, BamHI and XbaI correspond to the restriction enzyme sites on the bacterial expression vector pQE-9. (Qiagen, Inc., Chatsworth, CA). This plasmid vector encodes antibiotic resistance (Amp^r), a bacterial origin of replication (ori), an IPTG-regulatable promoter/operator (P/O), a ribosome binding site (RBS), a 6-histidine tag (6-His), and restriction enzyme cloning sites.

The pQE-9 vector is digested with BamHI and XbaI and the amplified fragment is ligated into the pQE-9 vector maintaining the reading frame initiated at the bacterial RBS. The ligation mixture is then used to transform the E. coli strain M15/rep4 (Qiagen, Inc.) which contains multiple copies of the plasmid pREP4, which expresses the lacI repressor and also confers kanamycin resistance (Kan^r). Transformants are identified by their ability to grow on LB plates and ampicillin/kanamycin resistant colonies are selected. Plasmid DNA is isolated and confirmed by restriction analysis.

Clones containing the desired constructs are grown overnight (O/N) in liquid culture in LB media supplemented with both Amp (100 ug/ml) and Kan (25 ug/ml). The O/N culture is used to inoculate a large culture at a ratio of 1:100 to 1:250. The cells are grown to an optical density 600 ($O.D.^{600}$) of between 0.4 and 0.6. IPTG (Isopropyl-B-D-thiogalacto pyranoside) is then added to a final concentration of 1 mM. IPTG induces by inactivating the lacI repressor, clearing the P/O leading to increased gene expression.

Cells are grown for an extra 3 to 4 hours. Cells are then harvested by centrifugation (20 mins at 6000Xg). The cell pellet is solubilized in the chaotropic agent 6 Molar Guanidine HCl by stirring for 3-4 hours at 4°C. The cell debris is removed by centrifugation, and the supernatant containing the polypeptide is loaded onto a nickel-nitrilo-tri-acetic acid ("Ni-NTA") affinity resin column (available from QIAGEN, Inc., *supra*). Proteins with a 6 x His tag bind to the Ni-NTA resin with high

affinity and can be purified in a simple one-step procedure (for details see: The QIAexpressionist (1995) QIAGEN, Inc., *supra*).

Briefly, the supernatant is loaded onto the column in 6 M guanidine-HCl, pH 8, the column is first washed with 10 volumes of 6 M guanidine-HCl, pH 8, then washed with 10 volumes of 6 M guanidine-HCl pH 6, and finally the polypeptide is eluted with 6 M guanidine-HCl, pH 5.

The purified protein is then renatured by dialyzing it against phosphate-buffered saline (PBS) or 50 mM Na-acetate, pH 6 buffer plus 200 mM NaCl. Alternatively, the protein can be successfully refolded while immobilized on the Ni-NTA column. The recommended conditions are as follows: renature using a linear 6M-1M urea gradient in 500 mM NaCl, 20% glycerol, 20 mM Tris/HCl pH 7.4, containing protease inhibitors. The renaturation should be performed over a period of 1.5 hours or more. After renaturation the proteins are eluted by the addition of 250 mM immidazole. Immidazole is removed by a final dialyzing step against PBS or 50 mM sodium acetate pH 6 buffer plus 200 mM NaCl. The purified protein is stored at 4°C or frozen at -80°C.

In addition to the above expression vector, the present invention further includes an expression vector comprising phage operator and promoter elements operatively linked to a polynucleotide of the present invention, called pHE4a. (ATCC Accession Number 209645, deposited on February 25, 1998.) This vector contains: 1) a neomycinphosphotransferase gene as a selection marker, 2) an E. coli origin of replication, 3) a T5 phage promoter sequence, 4) two lac operator sequences, 5) a Shine-Delgarno sequence, and 6) the lactose operon repressor gene (lacIq). The origin of replication (oriC) is derived from pUC19 (LTI, Gaithersburg, MD). The promoter sequence and operator sequences are made synthetically.

DNA can be inserted into the pHEa by restricting the vector with NdeI and XbaI, BamHI, XhoI, or Asp718, running the restricted product on a gel, and isolating the larger fragment (the stuffer fragment should be about 310 base pairs). The DNA insert is generated according to the PCR protocol described in Example 1, using PCR primers having restriction sites for NdeI (5' primer) and XbaI, BamHI, XhoI, or Asp718 (3' primer). The PCR insert is gel purified and restricted with compatible enzymes. The insert and vector are ligated according to standard protocols.

The engineered vector could easily be substituted in the above protocol to express protein in a bacterial system.

Example 6: Purification of a Polypeptide from an Inclusion Body

The following alternative method can be used to purify a polypeptide expressed in *E coli* when it is present in the form of inclusion bodies. Unless otherwise specified, all of the following steps are conducted at 4-10°C.

Upon completion of the production phase of the *E. coli* fermentation, the cell culture is cooled to 4-10°C and the cells harvested by continuous centrifugation at 15,000 rpm (Heraeus Sepatech). On the basis of the expected yield of protein per unit weight of cell paste and the amount of purified protein required, an appropriate amount of cell paste, by weight, is suspended in a buffer solution containing 100 mM Tris, 50 mM EDTA, pH 7.4. The cells are dispersed to a homogeneous suspension using a high shear mixer.

The cells are then lysed by passing the solution through a microfluidizer (Microfuidics, Corp. or APV Gaulin, Inc.) twice at 4000-6000 psi. The homogenate is then mixed with NaCl solution to a final concentration of 0.5 M NaCl, followed by centrifugation at 7000 xg for 15 min. The resultant pellet is washed again using 0.5M NaCl, 100 mM Tris, 50 mM EDTA, pH 7.4.

The resulting washed inclusion bodies are solubilized with 1.5 M guanidine hydrochloride (GuHCl) for 2-4 hours. After 7000 xg centrifugation for 15 min., the pellet is discarded and the polypeptide containing supernatant is incubated at 4°C overnight to allow further GuHCl extraction.

Following high speed centrifugation (30,000 xg) to remove insoluble particles, the GuHCl solubilized protein is refolded by quickly mixing the GuHCl extract with 20 volumes of buffer containing 50 mM sodium, pH 4.5, 150 mM NaCl, 2 mM EDTA by vigorous stirring. The refolded diluted protein solution is kept at 4°C without mixing for 12 hours prior to further purification steps.

To clarify the refolded polypeptide solution, a previously prepared tangential filtration unit equipped with 0.16 µm membrane filter with appropriate surface area (e.g., Filtron), equilibrated with 40 mM sodium acetate, pH 6.0 is employed. The filtered sample is loaded onto a cation exchange resin (e.g., Poros HS-50, Perseptive Biosystems). The column is washed with 40 mM sodium acetate, pH 6.0 and eluted with 250 mM, 500 mM, 1000 mM, and 1500 mM NaCl in the same buffer, in a stepwise manner. The absorbance at 280 nm of the effluent is continuously monitored. Fractions are collected and further analyzed by SDS-PAGE.

Fractions containing the polypeptide are then pooled and mixed with 4 volumes of water. The diluted sample is then loaded onto a previously prepared set of tandem

columns of strong anion (Poros HQ-50, Perseptive Biosystems) and weak anion (Poros CM-20, Perseptive Biosystems) exchange resins. The columns are equilibrated with 40 mM sodium acetate, pH 6.0. Both columns are washed with 40 mM sodium acetate, pH 6.0, 200 mM NaCl. The CM-20 column is then eluted using a 10 column volume linear gradient ranging from 0.2 M NaCl, 50 mM sodium acetate, pH 6.0 to 1.0 M NaCl, 50 mM sodium acetate, pH 6.5. Fractions are collected under constant A_{280} monitoring of the effluent. Fractions containing the polypeptide (determined, for instance, by 16% SDS-PAGE) are then pooled.

The resultant polypeptide should exhibit greater than 95% purity after the above refolding and purification steps. No major contaminant bands should be observed from Commassie blue stained 16% SDS-PAGE gel when 5 µg of purified protein is loaded. The purified protein can also be tested for endotoxin/LPS contamination, and typically the LPS content is less than 0.1 ng/ml according to LAL assays.

Example 7: Cloning and Expression of a Polypeptide in a Baculovirus Expression System

In this example, the plasmid shuttle vector pA2 is used to insert a polynucleotide into a baculovirus to express a polypeptide. This expression vector contains the strong polyhedrin promoter of the *Autographa californica* nuclear polyhedrosis virus (AcMNPV) followed by convenient restriction sites such as BamHI, Xba I and Asp718. The polyadenylation site of the simian virus 40 ("SV40") is used for efficient polyadenylation. For easy selection of recombinant virus, the plasmid contains the beta-galactosidase gene from *E. coli* under control of a weak Drosophila promoter in the same orientation, followed by the polyadenylation signal of the polyhedrin gene. The inserted genes are flanked on both sides by viral sequences for cell-mediated homologous recombination with wild-type viral DNA to generate a viable virus that express the cloned polynucleotide.

Many other baculovirus vectors can be used in place of the vector above, such as pAc373, pVL941, and pAcIM1, as one skilled in the art would readily appreciate, as long as the construct provides appropriately located signals for transcription, translation, secretion and the like, including a signal peptide and an in-frame AUG as required. Such vectors are described, for instance, in Luckow et al., Virology 170:31-39 (1989).

Specifically, the cDNA sequence contained in the deposited clone, including the AUG initiation codon and the naturally associated leader sequence identified in Table 1, is amplified using the PCR protocol described in Example 1. If the naturally occurring

signal sequence is used to produce the secreted protein, the pA2 vector does not need a second signal peptide. Alternatively, the vector can be modified (pA2 GP) to include a baculovirus leader sequence, using the standard methods described in Summers et al., "A Manual of Methods for Baculovirus Vectors and Insect Cell Culture Procedures," Texas Agricultural Experimental Station Bulletin No. 1555 (1987).

The amplified fragment is isolated from a 1% agarose gel using a commercially available kit ("Geneclean," BIO 101 Inc., La Jolla, Ca.). The fragment then is digested with appropriate restriction enzymes and again purified on a 1% agarose gel.

The plasmid is digested with the corresponding restriction enzymes and optionally, can be dephosphorylated using calf intestinal phosphatase, using routine procedures known in the art. The DNA is then isolated from a 1% agarose gel using a commercially available kit ("Geneclean" BIO 101 Inc., La Jolla, Ca.).

The fragment and the dephosphorylated plasmid are ligated together with T4 DNA ligase. *E. coli* HB101 or other suitable *E. coli* hosts such as XL-1 Blue (Stratagene Cloning Systems, La Jolla, CA) cells are transformed with the ligation mixture and spread on culture plates. Bacteria containing the plasmid are identified by digesting DNA from individual colonies and analyzing the digestion product by gel electrophoresis. The sequence of the cloned fragment is confirmed by DNA sequencing.

Five µg of a plasmid containing the polynucleotide is co-transfected with 1.0 µg of a commercially available linearized baculovirus DNA ("BaculoGold™ baculovirus DNA", Pharmingen, San Diego, CA), using the lipofection method described by Felgner et al., Proc. Natl. Acad. Sci. USA 84:7413-7417 (1987). One µg of BaculoGold™ virus DNA and 5 µg of the plasmid are mixed in a sterile well of a microtiter plate containing 50 µl of serum-free Grace's medium (Life Technologies Inc., Gaithersburg, MD). Afterwards, 10 µl Lipofectin plus 90 µl Grace's medium are added, mixed and incubated for 15 minutes at room temperature. Then the transfection mixture is added drop-wise to Sf9 insect cells (ATCC CRL 1711) seeded in a 35 mm tissue culture plate with 1 ml Grace's medium without serum. The plate is then incubated for 5 hours at 27° C. The transfection solution is then removed from the plate and 1 ml of Grace's insect medium supplemented with 10% fetal calf serum is added. Cultivation is then continued at 27° C for four days.

After four days the supernatant is collected and a plaque assay is performed, as described by Summers and Smith, *supra*. An agarose gel with "Blue Gal" (Life Technologies Inc., Gaithersburg) is used to allow easy identification and isolation of gal-expressing clones, which produce blue-stained plaques. (A detailed description of a "plaque assay" of this type can also be found in the user's guide for insect cell culture

and baculovirology distributed by Life Technologies Inc., Gaithersburg, page 9-10.) After appropriate incubation, blue stained plaques are picked with the tip of a micropipettor (e.g., Eppendorf). The agar containing the recombinant viruses is then resuspended in a microcentrifuge tube containing 200 µl of Grace's medium and the suspension containing the recombinant baculovirus is used to infect Sf9 cells seeded in 35 mm dishes. Four days later the supernatants of these culture dishes are harvested and then they are stored at 4° C.

To verify the expression of the polypeptide, Sf9 cells are grown in Grace's medium supplemented with 10% heat-inactivated FBS. The cells are infected with the recombinant baculovirus containing the polynucleotide at a multiplicity of infection ("MOI") of about 2. If radiolabeled proteins are desired, 6 hours later the medium is removed and is replaced with SF900 II medium minus methionine and cysteine (available from Life Technologies Inc., Rockville, MD). After 42 hours, 5 µCi of ^{35}S-methionine and 5 µCi ^{35}S-cysteine (available from Amersham) are added. The cells are further incubated for 16 hours and then are harvested by centrifugation. The proteins in the supernatant as well as the intracellular proteins are analyzed by SDS-PAGE followed by autoradiography (if radiolabeled).

Microsequencing of the amino acid sequence of the amino terminus of purified protein may be used to determine the amino terminal sequence of the produced protein.

Example 8: Expression of a Polypeptide in Mammalian Cells

The polypeptide of the present invention can be expressed in a mammalian cell. A typical mammalian expression vector contains a promoter element, which mediates the initiation of transcription of mRNA, a protein coding sequence, and signals required for the termination of transcription and polyadenylation of the transcript. Additional elements include enhancers, Kozak sequences and intervening sequences flanked by donor and acceptor sites for RNA splicing. Highly efficient transcription is achieved with the early and late promoters from SV40, the long terminal repeats (LTRs) from Retroviruses, e.g., RSV, HTLVI, HIVI and the early promoter of the cytomegalovirus (CMV). However, cellular elements can also be used (e.g., the human actin promoter).

Suitable expression vectors for use in practicing the present invention include, for example, vectors such as pSVL and pMSG (Pharmacia, Uppsala, Sweden), pRSVcat (ATCC 37152), pSV2dhfr (ATCC 37146), pBC12MI (ATCC 67109), pCMVSport 2.0, and pCMVSport 3.0. Mammalian host cells that could be used include, human Hela, 293, H9 and Jurkat cells, mouse NIH3T3 and C127 cells, Cos 1, Cos 7 and CV1, quail QC1-3 cells, mouse L cells and Chinese hamster ovary (CHO) cells.

Alternatively, the polypeptide can be expressed in stable cell lines containing the polynucleotide integrated into a chromosome. The co-transfection with a selectable marker such as dhfr, gpt, neomycin, hygromycin allows the identification and isolation of the transfected cells.

The transfected gene can also be amplified to express large amounts of the encoded protein. The DHFR (dihydrofolate reductase) marker is useful in developing cell lines that carry several hundred or even several thousand copies of the gene of interest. (See, e.g., Alt, F. W., et al., J. Biol. Chem. 253:1357-1370 (1978); Hamlin, J. L. and Ma, C., Biochem. et Biophys. Acta, 1097:107-143 (1990); Page, M. J. and Sydenham, M. A., Biotechnology 9:64-68 (1991).) Another useful selection marker is the enzyme glutamine synthase (GS) (Murphy et al., Biochem J. 227:277-279 (1991); Bebbington et al., Bio/Technology 10:169-175 (1992). Using these markers, the mammalian cells are grown in selective medium and the cells with the highest resistance are selected. These cell lines contain the amplified gene(s) integrated into a chromosome. Chinese hamster ovary (CHO) and NSO cells are often used for the production of proteins.

Derivatives of the plasmid pSV2-dhfr (ATCC Accession No. 37146), the expression vectors pC4 (ATCC Accession No. 209646) and pC6 (ATCC Accession No.209647) contain the strong promoter (LTR) of the Rous Sarcoma Virus (Cullen et al., Molecular and Cellular Biology, 438-447 (March, 1985)) plus a fragment of the CMV-enhancer (Boshart et al., Cell 41:521-530 (1985).) Multiple cloning sites, e.g., with the restriction enzyme cleavage sites BamHI, XbaI and Asp718, facilitate the cloning of the gene of interest. The vectors also contain the 3' intron, the polyadenylation and termination signal of the rat preproinsulin gene, and the mouse DHFR gene under control of the SV40 early promoter.

Specifically, the plasmid pC6, for example, is digested with appropriate restriction enzymes and then dephosphorylated using calf intestinal phosphates by procedures known in the art. The vector is then isolated from a 1% agarose gel.

A polynucleotide of the present invention is amplified according to the protocol outlined in Example 1. If the naturally occurring signal sequence is used to produce the secreted protein, the vector does not need a second signal peptide. Alternatively, if the naturally occurring signal sequence is not used, the vector can be modified to include a heterologous signal sequence. (See, e.g., WO 96/34891.)

The amplified fragment is isolated from a 1% agarose gel using a commercially available kit ("Geneclean," BIO 101 Inc., La Jolla, Ca.). The fragment then is digested with appropriate restriction enzymes and again purified on a 1% agarose gel.

The amplified fragment is then digested with the same restriction enzyme and purified on a 1% agarose gel. The isolated fragment and the dephosphorylated vector are then ligated with T4 DNA ligase. *E. coli* HB101 or XL-1 Blue cells are then transformed and bacteria are identified that contain the fragment inserted into plasmid pC6 using, for instance, restriction enzyme analysis.

Chinese hamster ovary cells lacking an active DHFR gene is used for transfection. Five µg of the expression plasmid pC6 is cotransfected with 0.5 µg of the plasmid pSVneo using lipofectin (Felgner et al., *supra*). The plasmid pSV2-neo contains a dominant selectable marker, the *neo* gene from Tn5 encoding an enzyme that confers resistance to a group of antibiotics including G418. The cells are seeded in alpha minus MEM supplemented with 1 mg/ml G418. After 2 days, the cells are trypsinized and seeded in hybridoma cloning plates (Greiner, Germany) in alpha minus MEM supplemented with 10, 25, or 50 ng/ml of metothrexate plus 1 mg/ml G418. After about 10-14 days single clones are trypsinized and then seeded in 6-well petri dishes or 10 ml flasks using different concentrations of methotrexate (50 nM, 100 nM, 200 nM, 400 nM, 800 nM). Clones growing at the highest concentrations of methotrexate are then transferred to new 6-well plates containing even higher concentrations of methotrexate (1 µM, 2 µM, 5 µM, 10 mM, 20 mM). The same procedure is repeated until clones are obtained which grow at a concentration of 100 - 200 µM. Expression of the desired gene product is analyzed, for instance, by SDS-PAGE and Western blot or by reversed phase HPLC analysis.

Example 9: Protein Fusions

The polypeptides of the present invention are preferably fused to other proteins. These fusion proteins can be used for a variety of applications. For example, fusion of the present polypeptides to His-tag, HA-tag, protein A, IgG domains, and maltose binding protein facilitates purification. (See Example 5; see also EP A 394,827; Traunecker, et al., Nature 331:84-86 (1988).) Similarly, fusion to IgG-1, IgG-3, and albumin increases the halflife time in vivo. Nuclear localization signals fused to the polypeptides of the present invention can target the protein to a specific subcellular localization, while covalent heterodimer or homodimers can increase or decrease the activity of a fusion protein. Fusion proteins can also create chimeric molecules having more than one function. Finally, fusion proteins can increase solubility and/or stability of the fused protein compared to the non-fused protein. All of the types of fusion proteins described above can be made by modifying the following protocol, which outlines the fusion of a polypeptide to an IgG molecule, or the protocol described in Example 5.

Briefly, the human Fc portion of the IgG molecule can be PCR amplified, using primers that span the 5' and 3' ends of the sequence described below. These primers also should have convenient restriction enzyme sites that will facilitate cloning into an expression vector, preferably a mammalian expression vector.

For example, if pC4 (Accession No. 209646) is used, the human Fc portion can be ligated into the BamHI cloning site. Note that the 3' BamHI site should be destroyed. Next, the vector containing the human Fc portion is re-restricted with BamHI, linearizing the vector, and a polynucleotide of the present invention, isolated by the PCR protocol described in Example 1, is ligated into this BamHI site. Note that the polynucleotide is cloned without a stop codon, otherwise a fusion protein will not be produced.

If the naturally occurring signal sequence is used to produce the secreted protein, pC4 does not need a second signal peptide. Alternatively, if the naturally occurring signal sequence is not used, the vector can be modified to include a heterologous signal sequence. (See, e.g., WO 96/34891.)

Human IgG Fc region:

GGGATCCGGAGCCCAAATCTTCTGACAAAACTCACACATGCCCACCGTGCC
CAGCACCTGAATTCGAGGGTGCACCGTCAGTCTTCCTCTTCCCCCCAAAACC
CAAGGACACCCTCATGATCTCCCGGACTCCTGAGGTCACATGCGTGGTGGT
GGACGTAAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACG
GCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAAC
AGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTG
AATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAACCCCC
ATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGT
GTACACCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCT
GACCTGCCTGGTCAAAGGCTTCTATCCAAGCGACATCGCCGTGGAGTGGGA
GAGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGG
ACTCCGACGGCTCCTTCTTCCTCTACAGCAAGCTCACCGTGGACAAGAGCA
GGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGC
ACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGGGTAAATGAGTGC
GACGGCCGCGACTCTAGAGGAT (SEQ ID NO:1)

Example 10: Production of an Antibody from a Polypeptide

The antibodies of the present invention can be prepared by a variety of methods. (See, Current Protocols, Chapter 2.) For example, cells expressing a polypeptide of the present invention is administered to an animal to induce the production of sera

containing polyclonal antibodies. In a preferred method, a preparation of the secreted protein is prepared and purified to render it substantially free of natural contaminants. Such a preparation is then introduced into an animal in order to produce polyclonal antisera of greater specific activity.

In the most preferred method, the antibodies of the present invention are monoclonal antibodies (or protein binding fragments thereof). Such monoclonal antibodies can be prepared using hybridoma technology. (Köhler et al., Nature 256:495 (1975); Köhler et al., Eur. J. Immunol. 6:511 (1976); Köhler et al., Eur. J. Immunol. 6:292 (1976); Hammerling et al., in: Monoclonal Antibodies and T-Cell Hybridomas, Elsevier, N.Y., pp. 563-681 (1981).) In general, such procedures involve immunizing an animal (preferably a mouse) with polypeptide or, more preferably, with a secreted polypeptide-expressing cell. Such cells may be cultured in any suitable tissue culture medium; however, it is preferable to culture cells in Earle's modified Eagle's medium supplemented with 10% fetal bovine serum (inactivated at about 56°C), and supplemented with about 10 g/l of nonessential amino acids, about 1,000 U/ml of penicillin, and about 100 µg/ml of streptomycin.

The splenocytes of such mice are extracted and fused with a suitable myeloma cell line. Any suitable myeloma cell line may be employed in accordance with the present invention; however, it is preferable to employ the parent myeloma cell line (SP2O), available from the ATCC. After fusion, the resulting hybridoma cells are selectively maintained in HAT medium, and then cloned by limiting dilution as described by Wands et al. (Gastroenterology 80:225-232 (1981).) The hybridoma cells obtained through such a selection are then assayed to identify clones which secrete antibodies capable of binding the polypeptide.

Alternatively, additional antibodies capable of binding to the polypeptide can be produced in a two-step procedure using anti-idiotypic antibodies. Such a method makes use of the fact that antibodies are themselves antigens, and therefore, it is possible to obtain an antibody which binds to a second antibody. In accordance with this method, protein specific antibodies are used to immunize an animal, preferably a mouse. The splenocytes of such an animal are then used to produce hybridoma cells, and the hybridoma cells are screened to identify clones which produce an antibody whose ability to bind to the protein-specific antibody can be blocked by the polypeptide. Such antibodies comprise anti-idiotypic antibodies to the protein-specific antibody and can be used to immunize an animal to induce formation of further protein-specific antibodies.

It will be appreciated that Fab and F(ab')2 and other fragments of the antibodies of the present invention may be used according to the methods disclosed herein. Such fragments are typically produced by proteolytic cleavage, using enzymes such as papain (to produce Fab fragments) or pepsin (to produce F(ab')2 fragments). Alternatively, secreted protein-binding fragments can be produced through the application of recombinant DNA technology or through synthetic chemistry.

For in vivo use of antibodies in humans, it may be preferable to use "humanized" chimeric monoclonal antibodies. Such antibodies can be produced using genetic constructs derived from hybridoma cells producing the monoclonal antibodies described above. Methods for producing chimeric antibodies are known in the art. (See, for review, Morrison, Science 229:1202 (1985); Oi et al., BioTechniques 4:214 (1986); Cabilly et al., U.S. Patent No. 4,816,567; Taniguchi et al., EP 171496; Morrison et al., EP 173494; Neuberger et al., WO 8601533; Robinson et al., WO 8702671; Boulianne et al., Nature 312:643 (1984); Neuberger et al., Nature 314:268 (1985).)

Example 11: Production Of Secreted Protein For High-Throughput Screening Assays

The following protocol produces a supernatant containing a polypeptide to be tested. This supernatant can then be used in the Screening Assays described in Examples 13-20.

First, dilute Poly-D-Lysine (644 587 Boehringer-Mannheim) stock solution (1mg/ml in PBS) 1:20 in PBS (w/o calcium or magnesium 17-516F Biowhittaker) for a working solution of 50ug/ml. Add 200 ul of this solution to each well (24 well plates) and incubate at RT for 20 minutes. Be sure to distribute the solution over each well (note: a 12-channel pipetter may be used with tips on every other channel). Aspirate off the Poly-D-Lysine solution and rinse with 1ml PBS (Phosphate Buffered Saline). The PBS should remain in the well until just prior to plating the cells and plates may be poly-lysine coated in advance for up to two weeks.

Plate 293T cells (do not carry cells past P+20) at 2 x 10^5 cells/well in .5ml DMEM(Dulbecco's Modified Eagle Medium)(with 4.5 G/L glucose and L-glutamine (12-604F Biowhittaker))/10% heat inactivated FBS(14-503F Biowhittaker)/1x Penstrep(17-602E Biowhittaker). Let the cells grow overnight.

The next day, mix together in a sterile solution basin: 300 ul Lipofectamine (18324-012 Gibco/BRL) and 5ml Optimem I (31985070 Gibco/BRL)/96-well plate. With a small volume multi-channel pipetter, aliquot approximately 2ug of an expression vector containing a polynucleotide insert, produced by the methods described in

Examples 8 or 9, into an appropriately labeled 96-well round bottom plate. With a multi-channel pipetter, add 50ul of the Lipofectamine/Optimem I mixture to each well. Pipette up and down gently to mix. Incubate at RT 15-45 minutes. After about 20 minutes, use a multi-channel pipetter to add 150ul Optimem I to each well. As a control, one plate of vector DNA lacking an insert should be transfected with each set of transfections.

Preferably, the transfection should be performed by tag-teaming the following tasks. By tag-teaming, hands on time is cut in half, and the cells do not spend too much time on PBS. First, person A aspirates off the media from four 24-well plates of cells, and then person B rinses each well with .5-1ml PBS. Person A then aspirates off PBS rinse, and person B, using a12-channel pipetter with tips on every other channel, adds the 200ul of DNA/Lipofectamine/Optimem I complex to the odd wells first, then to the even wells, to each row on the 24-well plates. Incubate at 37°C for 6 hours.

While cells are incubating, prepare appropriate media, either 1%BSA in DMEM with 1x penstrep, or CHO-5 media (116.6 mg/L of CaCl2 (anhyd); 0.00130 mg/L $CuSO_4$-$5H_2O$; 0.050 mg/L of $Fe(NO_3)_3$-$9H_2O$; 0.417 mg/L of $FeSO_4$-$7H_2O$; 311.80 mg/L of Kcl; 28.64 mg/L of $MgCl_2$; 48.84 mg/L of $MgSO_4$; 6995.50 mg/L of NaCl; 2400.0 mg/L of $NaHCO_3$; 62.50 mg/L of NaH_2PO_4-H_2O; 71.02 mg/L of Na_2HPO4; .4320 mg/L of $ZnSO_4$-$7H_2O$; .002 mg/L of Arachidonic Acid ; 1.022 mg/L of Cholesterol; .070 mg/L of DL-alpha-Tocopherol-Acetate; 0.0520 mg/L of Linoleic Acid; 0.010 mg/L of Linolenic Acid; 0.010 mg/L of Myristic Acid; 0.010 mg/L of Oleic Acid; 0.010 mg/L of Palmitric Acid; 0.010 mg/L of Palmitic Acid; 100 mg/L of Pluronic F-68; 0.010 mg/L of Stearic Acid; 2.20 mg/L of Tween 80; 4551 mg/L of D-Glucose; 130.85 mg/ml of L- Alanine; 147.50 mg/ml of L-Arginine-HCL; 7.50 mg/ml of L-Asparagine-H_2O; 6.65 mg/ml of L-Aspartic Acid; 29.56 mg/ml of L-Cystine-2HCL-H_2O; 31.29 mg/ml of L-Cystine-2HCL; 7.35 mg/ml of L-Glutamic Acid; 365.0 mg/ml of L-Glutamine; 18.75 mg/ml of Glycine; 52.48 mg/ml of L-Histidine-HCL-H_2O; 106.97 mg/ml of L-Isoleucine; 111.45 mg/ml of L-Leucine; 163.75 mg/ml of L-Lysine HCL; 32.34 mg/ml of L-Methionine; 68.48 mg/ml of L-Phenylalainine; 40.0 mg/ml of L-Proline; 26.25 mg/ml of L-Serine; 101.05 mg/ml of L-Threonine; 19.22 mg/ml of L-Tryptophan; 91.79 mg/ml of L-Tyrosine-2Na-$2H_2O$; 99.65 mg/ml of L-Valine; 0.0035 mg/L of Biotin; 3.24 mg/L of D-Ca Pantothenate; 11.78 mg/L of Choline Chloride; 4.65 mg/L of Folic Acid; 15.60 mg/L of i-Inositol; 3.02 mg/L of Niacinamide; 3.00 mg/L of Pyridoxal HCL; 0.031 mg/L of Pyridoxine HCL; 0.319 mg/L of Riboflavin; 3.17 mg/L of Thiamine HCL; 0.365 mg/L of Thymidine; and 0.680 mg/L of Vitamin B_{12}; 25 mM of HEPES Buffer; 2.39 mg/L of Na Hypoxanthine;

0.105 mg/L of Lipoic Acid; 0.081 mg/L of Sodium Putrescine-2HCL; 55.0 mg/L of Sodium Pyruvate; 0.0067 mg/L of Sodium Selenite; 20uM of Ethanolamine; 0.122 mg/L of Ferric Citrate; 41.70 mg/L of Methyl-B-Cyclodextrin complexed with Linoleic Acid; 33.33 mg/L of Methyl-B-Cyclodextrin complexed with Oleic Acid; and 10 mg/L of Methyl-B-Cyclodextrin complexed with Retinal) with 2mm glutamine and 1x penstrep. (BSA (81-068-3 Bayer) 100gm dissolved in 1L DMEM for a 10% BSA stock solution). Filter the media and collect 50 ul for endotoxin assay in 15ml polystyrene conical.

The transfection reaction is terminated, preferably by tag-teaming, at the end of the incubation period. Person A aspirates off the transfection media, while person B adds 1.5ml appropriate media to each well. Incubate at 37°C for 45 or 72 hours depending on the media used: 1%BSA for 45 hours or CHO-5 for 72 hours.

On day four, using a 300ul multichannel pipetter, aliquot 600ul in one 1ml deep well plate and the remaining supernatant into a 2ml deep well. The supernatants from each well can then be used in the assays described in Examples 13-20.

It is specifically understood that when activity is obtained in any of the assays described below using a supernatant, the activity originates from either the polypeptide directly (e.g., as a secreted protein) or by the polypeptide inducing expression of other proteins, which are then secreted into the supernatant. Thus, the invention further provides a method of identifying the protein in the supernatant characterized by an activity in a particular assay.

Example 12: Construction of GAS Reporter Construct

One signal transduction pathway involved in the differentiation and proliferation of cells is called the Jaks-STATs pathway. Activated proteins in the Jaks-STATs pathway bind to gamma activation site "GAS" elements or interferon-sensitive responsive element ("ISRE"), located in the promoter of many genes. The binding of a protein to these elements alter the expression of the associated gene.

GAS and ISRE elements are recognized by a class of transcription factors called Signal Transducers and Activators of Transcription, or "STATs." There are six members of the STATs family. Stat1 and Stat3 are present in many cell types, as is Stat2 (as response to IFN-alpha is widespread). Stat4 is more restricted and is not in many cell types though it has been found in T helper class I, cells after treatment with IL-12. Stat5 was originally called mammary growth factor, but has been found at higher concentrations in other cells including myeloid cells. It can be activated in tissue culture cells by many cytokines.

The STATs are activated to translocate from the cytoplasm to the nucleus upon tyrosine phosphorylation by a set of kinases known as the Janus Kinase ("Jaks") family. Jaks represent a distinct family of soluble tyrosine kinases and include Tyk2, Jak1, Jak2, and Jak3. These kinases display significant sequence similarity and are generally catalytically inactive in resting cells.

The Jaks are activated by a wide range of receptors summarized in the Table below. (Adapted from review by Schidler and Darnell, Ann. Rev. Biochem. 64:621-51 (1995).) A cytokine receptor family, capable of activating Jaks, is divided into two groups: (a) Class 1 includes receptors for IL-2, IL-3, IL-4, IL-6, IL-7, IL-9, IL-11, IL-12, IL-15, Epo, PRL, GH, G-CSF, GM-CSF, LIF, CNTF, and thrombopoietin; and (b) Class 2 includes IFN-a, IFN-g, and IL-10. The Class 1 receptors share a conserved cysteine motif (a set of four conserved cysteines and one tryptophan) and a WSXWS motif (a membrane proxial region encoding Trp-Ser-Xxx-Trp-Ser (SEQ ID NO:2)).

Thus, on binding of a ligand to a receptor, Jaks are activated, which in turn activate STATs, which then translocate and bind to GAS elements. This entire process is encompassed in the Jaks-STATs signal transduction pathway.

Therefore, activation of the Jaks-STATs pathway, reflected by the binding of the GAS or the ISRE element, can be used to indicate proteins involved in the proliferation and differentiation of cells. For example, growth factors and cytokines are known to activate the Jaks-STATs pathway. (See Table below.) Thus, by using GAS elements linked to reporter molecules, activators of the Jaks-STATs pathway can be identified.

	JAKs				STATS	GAS(elements) or ISRE
Ligand	tyk2	Jak1	Jak2	Jak3		
IFN family						
IFN-a/B	+	+	-	-	1,2,3	ISRE
IFN-g		+	+	-	1	GAS (IRF1>Lys6>IFP)
Il-10	+	?	?	-	1,3	
gp130 family						
IL-6 (Pleiotrohic)	+	+	+	?	1,3	GAS (IRF1>Lys6>IFP)
Il-11(Pleiotrohic)	?	+	?	?	1,3	
OnM(Pleiotrohic)	?	+	+	?	1,3	
LIF(Pleiotrohic)	?	+	+	?	1,3	
CNTF(Pleiotrohic)	-/+	+	+	?	1,3	
G-CSF(Pleiotrohic)	?	+	?	?	1,3	
IL-12(Pleiotrohic)	+	-	+	+	1,3	
g-C family						
IL-2 (lymphocytes)	-	+	-	+	1,3,5	GAS
IL-4 (lymph/myeloid)	-	+	-	+	6	GAS (IRF1 = IFP >>Ly6)(IgH)
IL-7 (lymphocytes)	-	+	-	+	5	GAS
IL-9 (lymphocytes)	-	+	-	+	5	GAS
IL-13 (lymphocyte)	-	+	?	?	6	GAS
IL-15	?	+	?	+	5	GAS
gp140 family						
IL-3 (myeloid)	-	-	+	-	5	GAS (IRF1>IFP>>Ly6)
IL-5 (myeloid)	-	-	+	-	5	GAS
GM-CSF (myeloid)	-	-	+	-	5	GAS
Growth hormone family						
GH	?	-	+	-	5	
PRL	?	+/-	+	-	1,3,5	
EPO	?	-	+	-	5	GAS(B-CAS>IRF1=IFP>>Ly6)
Receptor Tyrosine Kinases						
EGF	?	+	+	-	1,3	GAS (IRF1)
PDGF	?	+	+	-	1,3	
CSF-1	?	+	+	-	1,3	GAS (not IRF1)

To construct a synthetic GAS containing promoter element, which is used in the Biological Assays described in Examples 13-14, a PCR based strategy is employed to generate a GAS-SV40 promoter sequence. The 5' primer contains four tandem copies of the GAS binding site found in the IRF1 promoter and previously demonstrated to bind STATs upon induction with a range of cytokines (Rothman et al., Immunity 1:457-468 (1994).), although other GAS or ISRE elements can be used instead. The 5' primer also contains 18bp of sequence complementary to the SV40 early promoter sequence and is flanked with an XhoI site. The sequence of the 5' primer is:
5':GCGCCTCGAGATTTCCCCGAAATCTAGATTTCCCCGAAATGATTTCCCCG
AAATGATTTCCCCGAAATATCTGCCATCTCAATTAG:3' (SEQ ID NO:3)

The downstream primer is complementary to the SV40 promoter and is flanked with a Hind III site: 5':GCGGCAAGCTTTTTGCAAAGCCTAGGC:3' (SEQ ID NO:4)

PCR amplification is performed using the SV40 promoter template present in the B-gal:promoter plasmid obtained from Clontech. The resulting PCR fragment is digested with XhoI/Hind III and subcloned into BLSK2-. (Stratagene.) Sequencing with forward and reverse primers confirms that the insert contains the following sequence:
5':CTCGAGATTTCCCCGAAATCTAGATTTCCCCGAAATGATTTCCCCGAAATG
ATTTCCCCGAAATATCTGCCATCTCAATTAGTCAGCAACCATAGTCCCGCCC
CTAACTCCGCCCATCCCGCCCCTAACTCCGCCCAGTTCCGCCCATTCTCCGC
CCCATGGCTGACTAATTTTTTTTATTTATGCAGAGGCCGAGGCCGCCTCGGC
CTCTGAGCTATTCCAGAAGTAGTGAGGAGGCTTTTTTGGAGGCCTAGGCTTT
TGCAAAAAGCTT:3' (SEQ ID NO:5)

With this GAS promoter element linked to the SV40 promoter, a GAS:SEAP2 reporter construct is next engineered. Here, the reporter molecule is a secreted alkaline phosphatase, or "SEAP." Clearly, however, any reporter molecule can be instead of SEAP, in this or in any of the other Examples. Well known reporter molecules that can be used instead of SEAP include chloramphenicol acetyltransferase (CAT), luciferase, alkaline phosphatase, B-galactosidase, green fluorescent protein (GFP), or any protein detectable by an antibody.

The above sequence confirmed synthetic GAS-SV40 promoter element is subcloned into the pSEAP-Promoter vector obtained from Clontech using HindIII and XhoI, effectively replacing the SV40 promoter with the amplified GAS:SV40 promoter element, to create the GAS-SEAP vector. However, this vector does not contain a neomycin resistance gene, and therefore, is not preferred for mammalian expression systems.

Thus, in order to generate mammalian stable cell lines expressing the GAS-SEAP reporter, the GAS-SEAP cassette is removed from the GAS-SEAP vector using SalI and NotI, and inserted into a backbone vector containing the neomycin resistance gene, such as pGFP-1 (Clontech), using these restriction sites in the multiple cloning site, to create the GAS-SEAP/Neo vector. Once this vector is transfected into mammalian cells, this vector can then be used as a reporter molecule for GAS binding as described in Examples 13-14.

Other constructs can be made using the above description and replacing GAS with a different promoter sequence. For example, construction of reporter molecules containing NFK-B and EGR promoter sequences are described in Examples 15 and 16. However, many other promoters can be substituted using the protocols described in these Examples. For instance, SRE, IL-2, NFAT, or Osteocalcin promoters can be substituted, alone or in combination (e.g., GAS/NF-KB/EGR, GAS/NF-KB, Il-2/NFAT, or NF-KB/GAS). Similarly, other cell lines can be used to test reporter construct activity, such as HELA (epithelial), HUVEC (endothelial), Reh (B-cell), Saos-2 (osteoblast), HUVAC (aortic), or Cardiomyocyte.

Example 13: High-Throughput Screening Assay for T-cell Activity.

The following protocol is used to assess T-cell activity by identifying factors, such as growth factors and cytokines, that may proliferate or differentiate T-cells. T-cell activity is assessed using the GAS/SEAP/Neo construct produced in Example 12. Thus, factors that increase SEAP activity indicate the ability to activate the Jaks-STATS signal transduction pathway. The T-cell used in this assay is Jurkat T-cells (ATCC Accession No. TIB-152), although Molt-3 cells (ATCC Accession No. CRL-1552) and Molt-4 cells (ATCC Accession No. CRL-1582) cells can also be used.

Jurkat T-cells are lymphoblastic CD4+ Th1 helper cells. In order to generate stable cell lines, approximately 2 million Jurkat cells are transfected with the GAS-SEAP/neo vector using DMRIE-C (Life Technologies)(transfection procedure described below). The transfected cells are seeded to a density of approximately 20,000 cells per well and transfectants resistant to 1 mg/ml genticin selected. Resistant colonies are expanded and then tested for their response to increasing concentrations of interferon gamma. The dose response of a selected clone is demonstrated.

Specifically, the following protocol will yield sufficient cells for 75 wells containing 200 ul of cells. Thus, it is either scaled up, or performed in multiple to generate sufficient cells for multiple 96 well plates. Jurkat cells are maintained in RPMI + 10% serum with 1%Pen-Strep. Combine 2.5 mls of OPTI-MEM (Life Technologies)

with 10 ug of plasmid DNA in a T25 flask. Add 2.5 ml OPTI-MEM containing 50 ul of DMRIE-C and incubate at room temperature for 15-45 mins.

During the incubation period, count cell concentration, spin down the required number of cells (10^7 per transfection), and resuspend in OPTI-MEM to a final concentration of 10^7 cells/ml. Then add 1ml of 1 x 10^7 cells in OPTI-MEM to T25 flask and incubate at 37°C for 6 hrs. After the incubation, add 10 ml of RPMI + 15% serum.

The Jurkat:GAS-SEAP stable reporter lines are maintained in RPMI + 10% serum, 1 mg/ml Genticin, and 1% Pen-Strep. These cells are treated with supernatants containing a polypeptide as produced by the protocol described in Example 11.

On the day of treatment with the supernatant, the cells should be washed and resuspended in fresh RPMI + 10% serum to a density of 500,000 cells per ml. The exact number of cells required will depend on the number of supernatants being screened. For one 96 well plate, approximately 10 million cells (for 10 plates, 100 million cells) are required.

Transfer the cells to a triangular reservoir boat, in order to dispense the cells into a 96 well dish, using a 12 channel pipette. Using a 12 channel pipette, transfer 200 ul of cells into each well (therefore adding 100, 000 cells per well).

After all the plates have been seeded, 50 ul of the supernatants are transferred directly from the 96 well plate containing the supernatants into each well using a 12 channel pipette. In addition, a dose of exogenous interferon gamma (0.1, 1.0, 10 ng) is added to wells H9, H10, and H11 to serve as additional positive controls for the assay.

The 96 well dishes containing Jurkat cells treated with supernatants are placed in an incubator for 48 hrs (note: this time is variable between 48-72 hrs). 35 ul samples from each well are then transferred to an opaque 96 well plate using a 12 channel pipette. The opaque plates should be covered (using sellophene covers) and stored at -20°C until SEAP assays are performed according to Example 17. The plates containing the remaining treated cells are placed at 4°C and serve as a source of material for repeating the assay on a specific well if desired.

As a positive control, 100 Unit/ml interferon gamma can be used which is known to activate Jurkat T cells. Over 30 fold induction is typically observed in the positive control wells.

Example 14: High-Throughput Screening Assay Identifying Myeloid Activity

The following protocol is used to assess myeloid activity by identifying factors, such as growth factors and cytokines, that may proliferate or differentiate myeloid cells. Myeloid cell activity is assessed using the GAS/SEAP/Neo construct produced in Example 12. Thus, factors that increase SEAP activity indicate the ability to activate the Jaks-STATS signal transduction pathway. The myeloid cell used in this assay is U937, a pre-monocyte cell line, although TF-1, HL60, or KG1 can be used.

To transiently transfect U937 cells with the GAS/SEAP/Neo construct produced in Example 12, a DEAE-Dextran method (Kharbanda et. al., 1994, Cell Growth & Differentiation, 5:259-265) is used. First, harvest 2x10e^7 U937 cells and wash with PBS. The U937 cells are usually grown in RPMI 1640 medium containing 10% heat-inactivated fetal bovine serum (FBS) supplemented with 100 units/ml penicillin and 100 mg/ml streptomycin.

Next, suspend the cells in 1 ml of 20 mM Tris-HCl (pH 7.4) buffer containing 0.5 mg/ml DEAE-Dextran, 8 ug GAS-SEAP2 plasmid DNA, 140 mM NaCl, 5 mM KCl, 375 uM $Na_2HPO_4.7H_2O$, 1 mM $MgCl_2$, and 675 uM $CaCl_2$. Incubate at 37°C for 45 min.

Wash the cells with RPMI 1640 medium containing 10% FBS and then resuspend in 10 ml complete medium and incubate at 37°C for 36 hr.

The GAS-SEAP/U937 stable cells are obtained by growing the cells in 400 ug/ml G418. The G418-free medium is used for routine growth but every one to two months, the cells should be re-grown in 400 ug/ml G418 for couple of passages.

These cells are tested by harvesting 1x10^8 cells (this is enough for ten 96-well plates assay) and wash with PBS. Suspend the cells in 200 ml above described growth medium, with a final density of 5x10^5 cells/ml. Plate 200 ul cells per well in the 96-well plate (or 1x10^5 cells/well).

Add 50 ul of the supernatant prepared by the protocol described in Example 11. Incubate at 37°C for 48 to 72 hr. As a positive control, 100 Unit/ml interferon gamma can be used which is known to activate U937 cells. Over 30 fold induction is typically observed in the positive control wells. SEAP assay the supernatant according to the protocol described in Example 17.

Example 15: High-Throughput Screening Assay Identifying Neuronal Activity.

When cells undergo differentiation and proliferation, a group of genes are activated through many different signal transduction pathways. One of these genes, EGR1 (early growth response gene 1), is induced in various tissues and cell types upon

activation. The promoter of EGR1 is responsible for such induction. Using the EGR1 promoter linked to reporter molecules, activation of cells can be assessed.

Particularly, the following protocol is used to assess neuronal activity in PC12 cell lines. PC12 cells (rat phenochromocytoma cells) are known to proliferate and/or differentiate by activation with a number of mitogens, such as TPA (tetradecanoyl phorbol acetate), NGF (nerve growth factor), and EGF (epidermal growth factor). The EGR1 gene expression is activated during this treatment. Thus, by stably transfecting PC12 cells with a construct containing an EGR promoter linked to SEAP reporter, activation of PC12 cells can be assessed.

The EGR/SEAP reporter construct can be assembled by the following protocol. The EGR-1 promoter sequence (-633 to +1)(Sakamoto K et al., Oncogene 6:867-871 (1991)) can be PCR amplified from human genomic DNA using the following primers:

5' GCGCTCGAGGGATGACAGCGATAGAACCCCGG -3' (SEQ ID NO:6)

5' GCGAAGCTTCGCGACTCCCCGGATCCGCCTC-3' (SEQ ID NO:7)

Using the GAS:SEAP/Neo vector produced in Example 12, EGR1 amplified product can then be inserted into this vector. Linearize the GAS:SEAP/Neo vector using restriction enzymes XhoI/HindIII, removing the GAS/SV40 stuffer. Restrict the EGR1 amplified product with these same enzymes. Ligate the vector and the EGR1 promoter.

To prepare 96 well-plates for cell culture, two mls of a coating solution (1:30 dilution of collagen type I (Upstate Biotech Inc. Cat#08-115) in 30% ethanol (filter sterilized)) is added per one 10 cm plate or 50 ml per well of the 96-well plate, and allowed to air dry for 2 hr.

PC12 cells are routinely grown in RPMI-1640 medium (Bio Whittaker) containing 10% horse serum (JRH BIOSCIENCES, Cat. # 12449-78P), 5% heat-inactivated fetal bovine serum (FBS) supplemented with 100 units/ml penicillin and 100 ug/ml streptomycin on a precoated 10 cm tissue culture dish. One to four split is done every three to four days. Cells are removed from the plates by scraping and resuspended with pipetting up and down for more than 15 times.

Transfect the EGR/SEAP/Neo construct into PC12 using the Lipofectamine protocol described in Example 11. EGR-SEAP/PC12 stable cells are obtained by growing the cells in 300 ug/ml G418. The G418-free medium is used for routine growth but every one to two months, the cells should be re-grown in 300 ug/ml G418 for couple of passages.

To assay for neuronal activity, a 10 cm plate with cells around 70 to 80% confluent is screened by removing the old medium. Wash the cells once with PBS

(Phosphate buffered saline). Then starve the cells in low serum medium (RPMI-1640 containing 1% horse serum and 0.5% FBS with antibiotics) overnight.

The next morning, remove the medium and wash the cells with PBS. Scrape off the cells from the plate, suspend the cells well in 2 ml low serum medium. Count the cell number and add more low serum medium to reach final cell density as $5x10^5$ cells/ml.

Add 200 ul of the cell suspension to each well of 96-well plate (equivalent to $1x10^5$ cells/well). Add 50 ul supernatant produced by Example 11, 37°C for 48 to 72 hr. As a positive control, a growth factor known to activate PC12 cells through EGR can be used, such as 50 ng/ul of Neuronal Growth Factor (NGF). Over fifty-fold induction of SEAP is typically seen in the positive control wells. SEAP assay the supernatant according to Example 17.

Example 16: High-Throughput Screening Assay for T-cell Activity

NF-κB (Nuclear Factor κB) is a transcription factor activated by a wide variety of agents including the inflammatory cytokines IL-1 and TNF, CD30 and CD40, lymphotoxin-alpha and lymphotoxin-beta, by exposure to LPS or thrombin, and by expression of certain viral gene products. As a transcription factor, NF-κB regulates the expression of genes involved in immune cell activation, control of apoptosis (NF-κB appears to shield cells from apoptosis), B and T-cell development, anti-viral and antimicrobial responses, and multiple stress responses.

In non-stimulated conditions, NF- κB is retained in the cytoplasm with I-κB (Inhibitor κB). However, upon stimulation, I- κB is phosphorylated and degraded, causing NF- κB to shuttle to the nucleus, thereby activating transcription of target genes. Target genes activated by NF- κB include IL-2, IL-6, GM-CSF, ICAM-1 and class 1 MHC.

Due to its central role and ability to respond to a range of stimuli, reporter constructs utilizing the NF-κB promoter element are used to screen the supernatants produced in Example 11. Activators or inhibitors of NF-kB would be useful in treating diseases. For example, inhibitors of NF-κB could be used to treat those diseases related to the acute or chronic activation of NF-kB, such as rheumatoid arthritis.

To construct a vector containing the NF-κB promoter element, a PCR based strategy is employed. The upstream primer contains four tandem copies of the NF-κB binding site (GGGGACTTTCCC) (SEQ ID NO:8), 18 bp of sequence complementary to the 5' end of the SV40 early promoter sequence, and is flanked with an XhoI site:

5':GCGGCCTCGAGGGGACTTTCCCGGGGACTTTCCGGGGACTTTCCGGGAC TTTCCATCCTGCCATCTCAATTAG:3' (SEQ ID NO:9)

The downstream primer is complementary to the 3' end of the SV40 promoter and is flanked with a Hind III site:

5':GCGGCAAGCTTTTTGCAAAGCCTAGGC:3' (SEQ ID NO:4)

PCR amplification is performed using the SV40 promoter template present in the pB-gal:promoter plasmid obtained from Clontech. The resulting PCR fragment is digested with XhoI and Hind III and subcloned into BLSK2-. (Stratagene) Sequencing with the T7 and T3 primers confirms the insert contains the following sequence:

5':CTCGAGGGGACTTTCCCGGGGACTTTCCGGGGACTTTCCGGGACTTTCC ATCTGCCATCTCAATTAGTCAGCAACCATAGTCCCGCCCCTAACTCCGCCCA TCCCGCCCCTAACTCCGCCCAGTTCCGCCCATTCTCCGCCCCATGGCTGACT AATTTTTTTTATTTATGCAGAGGCCGAGGCCGCCTCGGCCTCTGAGCTATTC CAGAAGTAGTGAGGAGGCTTTTTTGGAGGCCTAGGCTTTTGCAAAAAGCTT: 3' (SEQ ID NO:10)

Next, replace the SV40 minimal promoter element present in the pSEAP2-promoter plasmid (Clontech) with this NF-κB/SV40 fragment using XhoI and HindIII. However, this vector does not contain a neomycin resistance gene, and therefore, is not preferred for mammalian expression systems.

In order to generate stable mammalian cell lines, the NF-κB/SV40/SEAP cassette is removed from the above NF-κB/SEAP vector using restriction enzymes SalI and NotI, and inserted into a vector containing neomycin resistance. Particularly, the NF-κB/SV40/SEAP cassette was inserted into pGFP-1 (Clontech), replacing the GFP gene, after restricting pGFP-1 with SalI and NotI.

Once NF-κB/SV40/SEAP/Neo vector is created, stable Jurkat T-cells are created and maintained according to the protocol described in Example 13. Similarly, the method for assaying supernatants with these stable Jurkat T-cells is also described

in Example 13. As a positive control, exogenous TNF alpha (0.1,1, 10 ng) is added to wells H9, H10, and H11, with a 5-10 fold activation typically observed.

Example 17: Assay for SEAP Activity

As a reporter molecule for the assays described in Examples 13-16, SEAP activity is assayed using the Tropix Phospho-light Kit (Cat. BP-400) according to the following general procedure. The Tropix Phospho-light Kit supplies the Dilution, Assay, and Reaction Buffers used below.

Prime a dispenser with the 2.5x Dilution Buffer and dispense 15 µl of 2.5x dilution buffer into Optiplates containing 35 µl of a supernatant. Seal the plates with a plastic sealer and incubate at 65°C for 30 min. Separate the Optiplates to avoid uneven heating.

Cool the samples to room temperature for 15 minutes. Empty the dispenser and prime with the Assay Buffer. Add 50 µl Assay Buffer and incubate at room temperature 5 min. Empty the dispenser and prime with the Reaction Buffer (see the table below). Add 50 µl Reaction Buffer and incubate at room temperature for 20 minutes. Since the intensity of the chemiluminescent signal is time dependent, and it takes about 10 minutes to read 5 plates on luminometer, one should treat 5 plates at each time and start the second set 10 minutes later.

Read the relative light unit in the luminometer. Set H12 as blank, and print the results. An increase in chemiluminescence indicates reporter activity.

Reaction Buffer Formulation:

# of plates	Rxn buffer diluent (ml)	CSPD (ml)
10	60	3
11	65	3.25
12	70	3.5
13	75	3.75
14	80	4
15	85	4.25
16	90	4.5
17	95	4.75
18	100	5
19	105	5.25
20	110	5.5
21	115	5.75
22	120	6
23	125	6.25
24	130	6.5
25	135	6.75
26	140	7
27	145	7.25

28	150	7.5
29	155	7.75
30	160	8
31	165	8.25
32	170	8.5
33	175	8.75
34	180	9
35	185	9.25
36	190	9.5
37	195	9.75
38	200	10
39	205	10.25
40	210	10.5
41	215	10.75
42	220	11
43	225	11.25
44	230	11.5
45	235	11.75
46	240	12
47	245	12.25
48	250	12.5
49	255	12.75
50	260	13

Example 18: High-Throughput Screening Assay Identifying Changes in Small Molecule Concentration and Membrane Permeability

Binding of a ligand to a receptor is known to alter intracellular levels of small molecules, such as calcium, potassium, sodium, and pH, as well as alter membrane potential. These alterations can be measured in an assay to identify supernatants which bind to receptors of a particular cell. Although the following protocol describes an assay for calcium, this protocol can easily be modified to detect changes in potassium, sodium, pH, membrane potential, or any other small molecule which is detectable by a fluorescent probe.

The following assay uses Fluorometric Imaging Plate Reader ("FLIPR") to measure changes in fluorescent molecules (Molecular Probes) that bind small molecules. Clearly, any fluorescent molecule detecting a small molecule can be used instead of the calcium fluorescent molecule, fluo-3, used here.

For adherent cells, seed the cells at 10,000 -20,000 cells/well in a Co-star black 96-well plate with clear bottom. The plate is incubated in a CO_2 incubator for 20 hours. The adherent cells are washed two times in Biotek washer with 200 ul of HBSS (Hank's Balanced Salt Solution) leaving 100 ul of buffer after the final wash.

A stock solution of 1 mg/ml fluo-3 is made in 10% pluronic acid DMSO. To load the cells with fluo-3, 50 ul of 12 ug/ml fluo-3 is added to each well. The plate is

incubated at 37°C in a CO_2 incubator for 60 min. The plate is washed four times in the Biotek washer with HBSS leaving 100 ul of buffer.

For non-adherent cells, the cells are spun down from culture media. Cells are re-suspended to 2-5x10^6 cells/ml with HBSS in a 50-ml conical tube. 4 ul of 1 mg/ml fluo-3 solution in 10% pluronic acid DMSO is added to each ml of cell suspension. The tube is then placed in a 37°C water bath for 30-60 min. The cells are washed twice with HBSS, resuspended to 1x10^6 cells/ml, and dispensed into a microplate, 100 ul/well. The plate is centrifuged at 1000 rpm for 5 min. The plate is then washed once in Denley CellWash with 200 ul, followed by an aspiration step to 100 ul final volume.

For a non-cell based assay, each well contains a fluorescent molecule, such as fluo-3. The supernatant is added to the well, and a change in fluorescence is detected.

To measure the fluorescence of intracellular calcium, the FLIPR is set for the following parameters: (1) System gain is 300-800 mW; (2) Exposure time is 0.4 second; (3) Camera F/stop is F/2; (4) Excitation is 488 nm; (5) Emission is 530 nm; and (6) Sample addition is 50 ul. Increased emission at 530 nm indicates an extracellular signaling event which has resulted in an increase in the intracellular Ca^{++} concentration.

Example 19: High-Throughput Screening Assay Identifying Tyrosine Kinase Activity

The Protein Tyrosine Kinases (PTK) represent a diverse group of transmembrane and cytoplasmic kinases. Within the Receptor Protein Tyrosine Kinase RPTK) group are receptors for a range of mitogenic and metabolic growth factors including the PDGF, FGF, EGF, NGF, HGF and Insulin receptor subfamilies. In addition there are a large family of RPTKs for which the corresponding ligand is unknown. Ligands for RPTKs include mainly secreted small proteins, but also membrane-bound and extracellular matrix proteins.

Activation of RPTK by ligands involves ligand-mediated receptor dimerization, resulting in transphosphorylation of the receptor subunits and activation of the cytoplasmic tyrosine kinases. The cytoplasmic tyrosine kinases include receptor associated tyrosine kinases of the src-family (e.g., src, yes, lck, lyn, fyn) and non-receptor linked and cytosolic protein tyrosine kinases, such as the Jak family, members of which mediate signal transduction triggered by the cytokine superfamily of receptors (e.g., the Interleukins, Interferons, GM-CSF, and Leptin).

Because of the wide range of known factors capable of stimulating tyrosine kinase activity, the identification of novel human secreted proteins capable of activating

tyrosine kinase signal transduction pathways are of interest. Therefore, the following protocol is designed to identify those novel human secreted proteins capable of activating the tyrosine kinase signal transduction pathways.

Seed target cells (e.g., primary keratinocytes) at a density of approximately 25,000 cells per well in a 96 well Loprodyne Silent Screen Plates purchased from Nalge Nunc (Naperville, IL). The plates are sterilized with two 30 minute rinses with 100% ethanol, rinsed with water and dried overnight. Some plates are coated for 2 hr with 100 ml of cell culture grade type I collagen (50 mg/ml), gelatin (2%) or polylysine (50 mg/ml), all of which can be purchased from Sigma Chemicals (St. Louis, MO) or 10% Matrigel purchased from Becton Dickinson (Bedford,MA), or calf serum, rinsed with PBS and stored at 4°C. Cell growth on these plates is assayed by seeding 5,000 cells/well in growth medium and indirect quantitation of cell number through use of alamarBlue as described by the manufacturer Alamar Biosciences, Inc. (Sacramento, CA) after 48 hr. Falcon plate covers #3071 from Becton Dickinson (Bedford,MA) are used to cover the Loprodyne Silent Screen Plates. Falcon Microtest III cell culture plates can also be used in some proliferation experiments.

To prepare extracts, A431 cells are seeded onto the nylon membranes of Loprodyne plates (20,000/200ml/well) and cultured overnight in complete medium. Cells are quiesced by incubation in serum-free basal medium for 24 hr. After 5-20 minutes treatment with EGF (60ng/ml) or 50 ul of the supernatant produced in Example 11, the medium was removed and 100 ml of extraction buffer ((20 mM HEPES pH 7.5, 0.15 M NaCl, 1% Triton X-100, 0.1% SDS, 2 mM Na3VO4, 2 mM Na4P2O7 and a cocktail of protease inhibitors (# 1836170) obtained from Boeheringer Mannheim (Indianapolis, IN) is added to each well and the plate is shaken on a rotating shaker for 5 minutes at 4°C. The plate is then placed in a vacuum transfer manifold and the extract filtered through the 0.45 mm membrane bottoms of each well using house vacuum. Extracts are collected in a 96-well catch/assay plate in the bottom of the vacuum manifold and immediately placed on ice. To obtain extracts clarified by centrifugation, the content of each well, after detergent solubilization for 5 minutes, is removed and centrifuged for 15 minutes at 4°C at 16,000 x g.

Test the filtered extracts for levels of tyrosine kinase activity. Although many methods of detecting tyrosine kinase activity are known, one method is described here.

Generally, the tyrosine kinase activity of a supernatant is evaluated by determining its ability to phosphorylate a tyrosine residue on a specific substrate (a biotinylated peptide). Biotinylated peptides that can be used for this purpose include PSK1 (corresponding to amino acids 6-20 of the cell division kinase cdc2-p34) and

PSK2 (corresponding to amino acids 1-17 of gastrin). Both peptides are substrates for a range of tyrosine kinases and are available from Boehringer Mannheim.

The tyrosine kinase reaction is set up by adding the following components in order. First, add 10ul of 5uM Biotinylated Peptide, then 10ul ATP/Mg_{2+} (5mM ATP/50mM $MgCl_2$), then 10ul of 5x Assay Buffer (40mM imidazole hydrochloride, pH7.3, 40 mM beta-glycerophosphate, 1mM EGTA, 100mM $MgCl_2$, 5 mM $MnCl_2$, 0.5 mg/ml BSA), then 5ul of Sodium Vanadate(1mM), and then 5ul of water. Mix the components gently and preincubate the reaction mix at 30°C for 2 min. Initial the reaction by adding 10ul of the control enzyme or the filtered supernatant.

The tyrosine kinase assay reaction is then terminated by adding 10 ul of 120mm EDTA and place the reactions on ice.

Tyrosine kinase activity is determined by transferring 50 ul aliquot of reaction mixture to a microtiter plate (MTP) module and incubating at 37°C for 20 min. This allows the streptavadin coated 96 well plate to associate with the biotinylated peptide. Wash the MTP module with 300ul/well of PBS four times. Next add 75 ul of anti-phospotyrosine antibody conjugated to horse radish peroxidase(anti-P-Tyr-POD(0.5u/ml)) to each well and incubate at 37°C for one hour. Wash the well as above.

Next add 100ul of peroxidase substrate solution (Boehringer Mannheim) and incubate at room temperature for at least 5 mins (up to 30 min). Measure the absorbance of the sample at 405 nm by using ELISA reader. The level of bound peroxidase activity is quantitated using an ELISA reader and reflects the level of tyrosine kinase activity.

Example 20: High-Throughput Screening Assay Identifying Phosphorylation Activity

As a potential alternative and/or compliment to the assay of protein tyrosine kinase activity described in Example 19, an assay which detects activation (phosphorylation) of major intracellular signal transduction intermediates can also be used. For example, as described below one particular assay can detect tyrosine phosphorylation of the Erk-1 and Erk-2 kinases. However, phosphorylation of other molecules, such as Raf, JNK, p38 MAP, Map kinase kinase (MEK), MEK kinase, Src, Muscle specific kinase (MuSK), IRAK, Tec, and Janus, as well as any other phosphoserine, phosphotyrosine, or phosphothreonine molecule, can be detected by substituting these molecules for Erk-1 or Erk-2 in the following assay.

Specifically, assay plates are made by coating the wells of a 96-well ELISA plate with 0.1ml of protein G (1ug/ml) for 2 hr at room temp, (RT). The plates are then rinsed with PBS and blocked with 3% BSA/PBS for 1 hr at RT. The protein G plates are then treated with 2 commercial monoclonal antibodies (100ng/well) against Erk-1 and Erk-2 (1 hr at RT) (Santa Cruz Biotechnology). (To detect other molecules, this step can easily be modified by substituting a monoclonal antibody detecting any of the above described molecules.) After 3-5 rinses with PBS, the plates are stored at 4°C until use.

A431 cells are seeded at 20,000/well in a 96-well Loprodyne filterplate and cultured overnight in growth medium. The cells are then starved for 48 hr in basal medium (DMEM) and then treated with EGF (6ng/well) or 50 ul of the supernatants obtained in Example 11 for 5-20 minutes. The cells are then solubilized and extracts filtered directly into the assay plate.

After incubation with the extract for 1 hr at RT, the wells are again rinsed. As a positive control, a commercial preparation of MAP kinase (10ng/well) is used in place of A431 extract. Plates are then treated with a commercial polyclonal (rabbit) antibody (1ug/ml) which specifically recognizes the phosphorylated epitope of the Erk-1 and Erk-2 kinases (1 hr at RT). This antibody is biotinylated by standard procedures. The bound polyclonal antibody is then quantitated by successive incubations with Europium-streptavidin and Europium fluorescence enhancing reagent in the Wallac DELFIA instrument (time-resolved fluorescence). An increased fluorescent signal over background indicates a phosphorylation.

Example 21: Method of Determining Alterations in a Gene Corresponding to a Polynucleotide

RNA isolated from entire families or individual patients presenting with a phenotype of interest (such as a disease) is be isolated. cDNA is then generated from these RNA samples using protocols known in the art. (See, Sambrook.) The cDNA is then used as a template for PCR, employing primers surrounding regions of interest in SEQ ID NO:X. Suggested PCR conditions consist of 35 cycles at 95°C for 30 seconds; 60-120 seconds at 52-58°C; and 60-120 seconds at 70°C, using buffer solutions described in Sidransky, D., et al., Science 252:706 (1991).

PCR products are then sequenced using primers labeled at their 5' end with T4 polynucleotide kinase, employing SequiTherm Polymerase. (Epicentre Technologies). The intron-exon borders of selected exons is also determined and genomic PCR

products analyzed to confirm the results. PCR products harboring suspected mutations is then cloned and sequenced to validate the results of the direct sequencing.

PCR products is cloned into T-tailed vectors as described in Holton, T.A. and Graham, M.W., Nucleic Acids Research, 19:1156 (1991) and sequenced with T7 polymerase (United States Biochemical). Affected individuals are identified by mutations not present in unaffected individuals.

Genomic rearrangements are also observed as a method of determining alterations in a gene corresponding to a polynucleotide. Genomic clones isolated according to Example 2 are nick-translated with digoxigenindeoxy-uridine 5'-triphosphate (Boehringer Manheim), and FISH performed as described in Johnson, Cg. et al., Methods Cell Biol. 35:73-99 (1991). Hybridization with the labeled probe is carried out using a vast excess of human cot-1 DNA for specific hybridization to the corresponding genomic locus.

Chromosomes are counterstained with 4,6-diamino-2-phenylidole and propidium iodide, producing a combination of C- and R-bands. Aligned images for precise mapping are obtained using a triple-band filter set (Chroma Technology, Brattleboro, VT) in combination with a cooled charge-coupled device camera (Photometrics, Tucson, AZ) and variable excitation wavelength filters. (Johnson, Cv. et al., Genet. Anal. Tech. Appl., 8:75 (1991).) Image collection, analysis and chromosomal fractional length measurements are performed using the ISee Graphical Program System. (Inovision Corporation, Durham, NC.) Chromosome alterations of the genomic region hybridized by the probe are identified as insertions, deletions, and translocations. These alterations are used as a diagnostic marker for an associated disease.

Example 22: Method of Detecting Abnormal Levels of a Polypeptide in a Biological Sample

A polypeptide of the present invention can be detected in a biological sample, and if an increased or decreased level of the polypeptide is detected, this polypeptide is a marker for a particular phenotype. Methods of detection are numerous, and thus, it is understood that one skilled in the art can modify the following assay to fit their particular needs.

For example, antibody-sandwich ELISAs are used to detect polypeptides in a sample, preferably a biological sample. Wells of a microtiter plate are coated with specific antibodies, at a final concentration of 0.2 to 10 ug/ml. The antibodies are either monoclonal or polyclonal and are produced by the method described in Example 10.

The wells are blocked so that non-specific binding of the polypeptide to the well is reduced.

The coated wells are then incubated for > 2 hours at RT with a sample containing the polypeptide. Preferably, serial dilutions of the sample should be used to validate results. The plates are then washed three times with deionized or distilled water to remove unbounded polypeptide.

Next, 50 ul of specific antibody-alkaline phosphatase conjugate, at a concentration of 25-400 ng, is added and incubated for 2 hours at room temperature. The plates are again washed three times with deionized or distilled water to remove unbounded conjugate.

Add 75 ul of 4-methylumbelliferyl phosphate (MUP) or p-nitrophenyl phosphate (NPP) substrate solution to each well and incubate 1 hour at room temperature. Measure the reaction by a microtiter plate reader. Prepare a standard curve, using serial dilutions of a control sample, and plot polypeptide concentration on the X-axis (log scale) and fluorescence or absorbance of the Y-axis (linear scale). Interpolate the concentration of the polypeptide in the sample using the standard curve.

Example 23: Formulating a Polypeptide

The secreted polypeptide composition will be formulated and dosed in a fashion consistent with good medical practice, taking into account the clinical condition of the individual patient (especially the side effects of treatment with the secreted polypeptide alone), the site of delivery, the method of administration, the scheduling of administration, and other factors known to practitioners. The "effective amount" for purposes herein is thus determined by such considerations.

As a general proposition, the total pharmaceutically effective amount of secreted polypeptide administered parenterally per dose will be in the range of about 1 µg/kg/day to 10 mg/kg/day of patient body weight, although, as noted above, this will be subject to therapeutic discretion. More preferably, this dose is at least 0.01 mg/kg/day, and most preferably for humans between about 0.01 and 1 mg/kg/day for the hormone. If given continuously, the secreted polypeptide is typically administered at a dose rate of about 1 µg/kg/hour to about 50 µg/kg/hour, either by 1-4 injections per day or by continuous subcutaneous infusions, for example, using a mini-pump. An intravenous bag solution may also be employed. The length of treatment needed to observe changes and the interval following treatment for responses to occur appears to vary depending on the desired effect.

Pharmaceutical compositions containing the secreted protein of the invention are administered orally, rectally, parenterally, intracistemally, intravaginally,

intraperitoneally, topically (as by powders, ointments, gels, drops or transdermal patch), bucally, or as an oral or nasal spray. "Pharmaceutically acceptable carrier" refers to a non-toxic solid, semisolid or liquid filler, diluent, encapsulating material or formulation auxiliary of any type. The term "parenteral" as used herein refers to modes of administration which include intravenous, intramuscular, intraperitoneal, intrasternal, subcutaneous and intraarticular injection and infusion.

The secreted polypeptide is also suitably administered by sustained-release systems. Suitable examples of sustained-release compositions include semi-permeable polymer matrices in the form of shaped articles, e.g., films, or mirocapsules. Sustained-release matrices include polylactides (U.S. Pat. No. 3,773,919, EP 58,481), copolymers of L-glutamic acid and gamma-ethyl-L-glutamate (Sidman, U. et al., Biopolymers 22:547-556 (1983)), poly (2- hydroxyethyl methacrylate) (R. Langer et al., J. Biomed. Mater. Res. 15:167-277 (1981), and R. Langer, Chem. Tech. 12:98-105 (1982)), ethylene vinyl acetate (R. Langer et al.) or poly-D- (-)-3-hydroxybutyric acid (EP 133,988). Sustained-release compositions also include liposomally entrapped polypeptides. Liposomes containing the secreted polypeptide are prepared by methods known per se: DE 3,218,121; Epstein et al., Proc. Natl. Acad. Sci. USA 82:3688-3692 (1985); Hwang et al., Proc. Natl. Acad. Sci. USA 77:4030-4034 (1980); EP 52,322; EP 36,676; EP 88,046; EP 143,949; EP 142,641; Japanese Pat. Appl. 83-118008; U.S. Pat. Nos. 4,485,045 and 4,544,545; and EP 102,324. Ordinarily, the liposomes are of the small (about 200-800 Angstroms) unilamellar type in which the lipid content is greater than about 30 mol. percent cholesterol, the selected proportion being adjusted for the optimal secreted polypeptide therapy.

For parenteral administration, in one embodiment, the secreted polypeptide is formulated generally by mixing it at the desired degree of purity, in a unit dosage injectable form (solution, suspension, or emulsion), with a pharmaceutically acceptable carrier, i.e., one that is non-toxic to recipients at the dosages and concentrations employed and is compatible with other ingredients of the formulation. For example, the formulation preferably does not include oxidizing agents and other compounds that are known to be deleterious to polypeptides.

Generally, the formulations are prepared by contacting the polypeptide uniformly and intimately with liquid carriers or finely divided solid carriers or both. Then, if necessary, the product is shaped into the desired formulation. Preferably the carrier is a parenteral carrier, more preferably a solution that is isotonic with the blood of the recipient. Examples of such carrier vehicles include water, saline, Ringer's solution, and dextrose solution. Non-aqueous vehicles such as fixed oils and ethyl oleate are also useful herein, as well as liposomes.

The carrier suitably contains minor amounts of additives such as substances that enhance isotonicity and chemical stability. Such materials are non-toxic to recipients at the dosages and concentrations employed, and include buffers such as phosphate, citrate, succinate, acetic acid, and other organic acids or their salts; antioxidants such as ascorbic acid; low molecular weight (less than about ten residues) polypeptides, e.g., polyarginine or tripeptides; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids, such as glycine, glutamic acid, aspartic acid, or arginine; monosaccharides, disaccharides, and other carbohydrates including cellulose or its derivatives, glucose, manose, or dextrins; chelating agents such as EDTA; sugar alcohols such as mannitol or sorbitol; counterions such as sodium; and/or nonionic surfactants such as polysorbates, poloxamers, or PEG.

The secreted polypeptide is typically formulated in such vehicles at a concentration of about 0.1 mg/ml to 100 mg/ml, preferably 1-10 mg/ml, at a pH of about 3 to 8. It will be understood that the use of certain of the foregoing excipients, carriers, or stabilizers will result in the formation of polypeptide salts.

Any polypeptide to be used for therapeutic administration can be sterile. Sterility is readily accomplished by filtration through sterile filtration membranes (e.g., 0.2 micron membranes). Therapeutic polypeptide compositions generally are placed into a container having a sterile access port, for example, an intravenous solution bag or vial having a stopper pierceable by a hypodermic injection needle.

Polypeptides ordinarily will be stored in unit or multi-dose containers, for example, sealed ampoules or vials, as an aqueous solution or as a lyophilized formulation for reconstitution. As an example of a lyophilized formulation, 10-ml vials are filled with 5 ml of sterile-filtered 1% (w/v) aqueous polypeptide solution, and the resulting mixture is lyophilized. The infusion solution is prepared by reconstituting the lyophilized polypeptide using bacteriostatic Water-for-Injection.

The invention also provides a pharmaceutical pack or kit comprising one or more containers filled with one or more of the ingredients of the pharmaceutical compositions of the invention. Associated with such container(s) can be a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration. In addition, the polypeptides of the present invention may be employed in conjunction with other therapeutic compounds.

Example 24: Method of Treating Decreased Levels of the Polypeptide

It will be appreciated that conditions caused by a decrease in the standard or normal expression level of a secreted protein in an individual can be treated by administering the polypeptide of the present invention, preferably in the secreted form. Thus, the invention also provides a method of treatment of an individual in need of an increased level of the polypeptide comprising administering to such an individual a pharmaceutical composition comprising an amount of the polypeptide to increase the activity level of the polypeptide in such an individual.

For example, a patient with decreased levels of a polypeptide receives a daily dose 0.1-100 ug/kg of the polypeptide for six consecutive days. Preferably, the polypeptide is in the secreted form. The exact details of the dosing scheme, based on administration and formulation, are provided in Example 23.

Example 25: Method of Treating Increased Levels of the Polypeptide

Antisense technology is used to inhibit production of a polypeptide of the present invention. This technology is one example of a method of decreasing levels of a polypeptide, preferably a secreted form, due to a variety of etiologies, such as cancer.

For example, a patient diagnosed with abnormally increased levels of a polypeptide is administered intravenously antisense polynucleotides at 0.5, 1.0, 1.5, 2.0 and 3.0 mg/kg day for 21 days. This treatment is repeated after a 7-day rest period if the treatment was well tolerated. The formulation of the antisense polynucleotide is provided in Example 23.

Example 26: Method of Treatment Using Gene Therapy

One method of gene therapy transplants fibroblasts, which are capable of expressing a polypeptide, onto a patient. Generally, fibroblasts are obtained from a subject by skin biopsy. The resulting tissue is placed in tissue-culture medium and separated into small pieces. Small chunks of the tissue are placed on a wet surface of a tissue culture flask, approximately ten pieces are placed in each flask. The flask is turned upside down, closed tight and left at room temperature over night. After 24 hours at room temperature, the flask is inverted and the chunks of tissue remain fixed to the bottom of the flask and fresh media (e.g., Ham's F12 media, with 10% FBS, penicillin and streptomycin) is added. The flasks are then incubated at 37°C for approximately one week.

At this time, fresh media is added and subsequently changed every several days. After an additional two weeks in culture, a monolayer of fibroblasts emerge. The monolayer is trypsinized and scaled into larger flasks.

pMV-7 (Kirschmeier, P.T. et al., DNA, 7:219-25 (1988)), flanked by the long terminal repeats of the Moloney murine sarcoma virus, is digested with EcoRI and HindIII and subsequently treated with calf intestinal phosphatase. The linear vector is fractionated on agarose gel and purified, using glass beads.

The cDNA encoding a polypeptide of the present invention can be amplified using PCR primers which correspond to the 5' and 3' end sequences respectively as set forth in Example 1. Preferably, the 5' primer contains an EcoRI site and the 3' primer includes a HindIII site. Equal quantities of the Moloney murine sarcoma virus linear backbone and the amplified EcoRI and HindIII fragment are added together, in the presence of T4 DNA ligase. The resulting mixture is maintained under conditions appropriate for ligation of the two fragments. The ligation mixture is then used to transform bacteria HB101, which are then plated onto agar containing kanamycin for the purpose of confirming that the vector has the gene of interest properly inserted.

The amphotropic pA317 or GP+am12 packaging cells are grown in tissue culture to confluent density in Dulbecco's Modified Eagles Medium (DMEM) with 10% calf serum (CS), penicillin and streptomycin. The MSV vector containing the gene is then added to the media and the packaging cells transduced with the vector. The packaging cells now produce infectious viral particles containing the gene (the packaging cells are now referred to as producer cells).

Fresh media is added to the transduced producer cells, and subsequently, the media is harvested from a 10 cm plate of confluent producer cells. The spent media, containing the infectious viral particles, is filtered through a millipore filter to remove detached producer cells and this media is then used to infect fibroblast cells. Media is removed from a sub-confluent plate of fibroblasts and quickly replaced with the media from the producer cells. This media is removed and replaced with fresh media. If the titer of virus is high, then virtually all fibroblasts will be infected and no selection is required. If the titer is very low, then it is necessary to use a retroviral vector that has a selectable marker, such as neo or his. Once the fibroblasts have been efficiently infected, the fibroblasts are analyzed to determine whether protein is produced.

The engineered fibroblasts are then transplanted onto the host, either alone or after having been grown to confluence on cytodex 3 microcarrier beads.

It will be clear that the invention may be practiced otherwise than as particularly described in the foregoing description and examples. Numerous modifications and variations of the present invention are possible in light of the above teachings and, therefore, are within the scope of the appended claims.

The entire disclosure of each document cited (including patents, patent applications, journal articles, abstracts, laboratory manuals, books, or other

disclosures) in the Background of the Invention, Detailed Description, and Examples is hereby incorporated herein by reference. Further, the hard copy of the sequence listing submitted herewith and the corresponding computer readable form are both incorporated herein by reference in their entireties.

305

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13*bis*)

A. The indications made below relate to the microorganism referred to in the description on page 212, line N/A.

B. IDENTIFICATION OF DEPOSIT — Further deposits are identified on an additional sheet [X]

Name of depositary institution: American Type Culture Collection ("ATCC")

Address of depositary institution *(including postal code and country)*:
10801 University Boulevard
Manassas, Virginia 20110-2209
United States of America

Date of deposit	Accession Number
25 SEPTEMBER 1997	209299

C. ADDITIONAL INDICATIONS *(leave blank if not applicable)* — This information is continued on an additional sheet [ ]

D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE *(if the indications are not for all designated States)*

E. SEPARATE FURNISHING OF INDICATIONS *(leave blank if not applicable)*

The indications listed below will be submitted to the International Bureau later *(specify the general nature of the indications e.g., "Accession Number of Deposit")*

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306

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13*bis*)

A. The indications made below relate to the microorganism referred to in the description on page 215, line N/A.

B. IDENTIFICATION OF DEPOSIT — Further deposits are identified on an additional sheet [X]

Name of depositary institution: American Type Culture Collection ("ATCC")

Address of depositary institution *(including postal code and country)*:
10801 University Boulevard
Manassas, Virginia 20110-2209
United States of America

Date of deposit	Accession Number
25 SEPTEMBER 1997	209300

C. ADDITIONAL INDICATIONS *(leave blank if not applicable)* — This information is continued on an additional sheet [ ]

D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE *(if the indications are not for all designated States)*

E. SEPARATE FURNISHING OF INDICATIONS *(leave blank if not applicable)*

The indications listed below will be submitted to the International Bureau later *(specify the general nature of the indications e.g., "Accession Number of Deposit")*

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307

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13*bis*)

A. The indications made below relate to the microorganism referred to in the description on page 220, line N/A

B. IDENTIFICATION OF DEPOSIT — Further deposits are identified on an additional sheet ☒

Name of depositary institution: American Type Culture Collection ("ATCC")

Address of depositary institution *(including postal code and country)*:
10801 University Boulevard
Manassas, Virginia 20110-2209
United States of America

Date of deposit	Accession Number
02 OCTOBER 1997	209324

C. ADDITIONAL INDICATIONS *(leave blank if not applicable)* — This information is continued on an additional sheet ☐

D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE *(if the indications are not for all designated States)*

E. SEPARATE FURNISHING OF INDICATIONS *(leave blank if not applicable)*

The indications listed below will be submitted to the International Bureau later *(specify the general nature of the indications e.g., "Accession Number of Deposit")*

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Authorized officer: Sonya Barnes, PCT International Division	Authorized officer

308

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13*bis*)

A. The indications made below relate to the microorganism referred to in the description on page 225, line N/A

B. IDENTIFICATION OF DEPOSIT — Further deposits are identified on an additional sheet ☐

Name of depositary institution: American Type Culture Collection ("ATCC")

Address of depositary institution *(including postal code and country)*:
10801 University Boulevard
Manassas, Virginia 20110-2209
United States of America

Date of deposit	Accession Number
09 OCTOBER 1997	209346

C. ADDITIONAL INDICATIONS *(leave blank if not applicable)* — This information is continued on an additional sheet ☐

D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE *(if the indications are not for all designated States)*

E. SEPARATE FURNISHING OF INDICATIONS *(leave blank if not applicable)*

The indications listed below will be submitted to the International Bureau later *(specify the general nature of the indications e.g., "Accession Number of Deposit")*

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Authorized officer: Sonya Barnes, PCT International Division	Authorized officer

What Is Claimed Is:

1. An isolated nucleic acid molecule comprising a polynucleotide having a nucleotide sequence at least 95% identical to a sequence selected from the group consisting of:

(a) a polynucleotide fragment of SEQ ID NO:X or a polynucleotide fragment of the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X;

(b) a polynucleotide encoding a polypeptide fragment of SEQ ID NO:Y or a polypeptide fragment encoded by the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X;

(c) a polynucleotide encoding a polypeptide domain of SEQ ID NO:Y or a polypeptide domain encoded by the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X;

(d) a polynucleotide encoding a polypeptide epitope of SEQ ID NO:Y or a polypeptide epitope encoded by the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X;

(e) a polynucleotide encoding a polypeptide of SEQ ID NO:Y or the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X, having biological activity;

(f) a polynucleotide which is a variant of SEQ ID NO:X;

(g) a polynucleotide which is an allelic variant of SEQ ID NO:X;

(h) a polynucleotide which encodes a species homologue of the SEQ ID NO:Y;

(i) a polynucleotide capable of hybridizing under stringent conditions to any one of the polynucleotides specified in (a)-(h), wherein said polynucleotide does not hybridize under stringent conditions to a nucleic acid molecule having a nucleotide sequence of only A residues or of only T residues.

2. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises a nucleotide sequence encoding a secreted protein.

3. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises a nucleotide sequence encoding the sequence identified as SEQ ID NO:Y or the polypeptide encoded by the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X.

4. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises the entire nucleotide sequence of SEQ ID NO:X or the cDNA sequence included in ATCC Deposit No:Z, which is hybridizable to SEQ ID NO:X.

5. The isolated nucleic acid molecule of claim 2, wherein the nucleotide sequence comprises sequential nucleotide deletions from either the C-terminus or the N-terminus.

6. The isolated nucleic acid molecule of claim 3, wherein the nucleotide sequence comprises sequential nucleotide deletions from either the C-terminus or the N-terminus.

7. A recombinant vector comprising the isolated nucleic acid molecule of claim 1.

8. A method of making a recombinant host cell comprising the isolated nucleic acid molecule of claim 1.

9. A recombinant host cell produced by the method of claim 8.

10. The recombinant host cell of claim 9 comprising vector sequences.

11. An isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence selected from the group consisting of:

(a) a polypeptide fragment of SEQ ID NO:Y or the encoded sequence included in ATCC Deposit No:Z;

(b) a polypeptide fragment of SEQ ID NO:Y or the encoded sequence included in ATCC Deposit No:Z, having biological activity;

(c) a polypeptide domain of SEQ ID NO:Y or the encoded sequence included in ATCC Deposit No:Z;

(d) a polypeptide epitope of SEQ ID NO:Y or the encoded sequence included in ATCC Deposit No:Z;

(e) a secreted form of SEQ ID NO:Y or the encoded sequence included in ATCC Deposit No:Z;

(f) a full length protein of SEQ ID NO:Y or the encoded sequence included in ATCC Deposit No:Z;

(g) a variant of SEQ ID NO:Y;

(h) an allelic variant of SEQ ID NO:Y; or

(i) a species homologue of the SEQ ID NO:Y.

12. The isolated polypeptide of claim 11, wherein the secreted form or the full length protein comprises sequential amino acid deletions from either the C-terminus or the N-terminus.

13. An isolated antibody that binds specifically to the isolated polypeptide of claim 11.

14. A recombinant host cell that expresses the isolated polypeptide of claim 11.

15. A method of making an isolated polypeptide comprising:

(a) culturing the recombinant host cell of claim 14 under conditions such that said polypeptide is expressed; and

(b) recovering said polypeptide.

16. The polypeptide produced by claim 15.

17. A method for preventing, treating, or ameliorating a medical condition, comprising administering to a mammalian subject a therapeutically effective amount of the polypeptide of claim 11 or the polynucleotide of claim 1.

18. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:

(a) determining the presence or absence of a mutation in the polynucleotide of claim 1; and

(b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or absence of said mutation.

19. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:

(a) determining the presence or amount of expression of the polypeptide of claim 11 in a biological sample; and

(b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or amount of expression of the polypeptide.

20. A method for identifying a binding partner to the polypeptide of claim 11 comprising:

(a) contacting the polypeptide of claim 11 with a binding partner; and

(b) determining whether the binding partner effects an activity of the polypeptide.

21. The gene corresponding to the cDNA sequence of SEQ ID NO:Y.

22. A method of identifying an activity in a biological assay, wherein the method comprises:

(a) expressing SEQ ID NO:X in a cell;

(b) isolating the supernatant;

(c) detecting an activity in a biological assay; and

(d) identifying the protein in the supernatant having the activity.

23. The product produced by the method of claim 20.

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agttttgtgt gttaagtctc gccatgcagt ggtcttaatc ttgttttcaa cttgtagctc 300
tgccatacct gtctctctaa ggagacctaa ctattgccta cttcccacct gcggccattc 360
atccaccagg cccaagctta tgggtgttga acaatacagc tacttatttt tgacatgtgt 420
ctttatgtgt gtgtcactcc agtggaagtc aacccaaccg tgggtaggag acantacntg 480
tatgaggaaa gggatcacag gtacagaagt tcacagaact aatgcacttt tcacattttg 540
gtgctcataa ngcatttccc cctatagata tgatttgaga nagaagacac tgaaagaatg 600
gaggaataga caccaagtta atargggttc ctaactgatg aatttcactc ttaggatggc 660
tgagccagag accaccattt cattcttttt gctgtgccct gcctgtttcg atggttttcc 720
aggattccca acgtgataag tgtgtcccag tgtgacgtta tttaatctat tctggcaatt 780
cagtgtcagt atccgttttc ccttcaaata tttcaccaaa gtatttatgc cccactactg 840
tatttcattg attgtaagat acacgctggt ttttattagc atttctgaag ttgaaatgcg 900
tggaacattg gtggtgtgtc ataatacttt aggatttgtt acttagtggt acaccaaata 960
atggtaggtt gatggtgttt tagattgcct cga 993

<210> 19
<211> 459
<212> DNA

<213> Homo sapiens

<400> 19
ggcacgagga agcgtgaacc ccagggaaca gcgggtccct tccctcctca gacacaagcc 60
acctcagctt gtggctcttg gccccccagcc ccaccaaccc acctgttcat ttattcaaca 120
gacaatgaca gctgatattt attggacatt tgcaccatgc caagcattcg gcttggatta 180
tcccatttgt ttctcacagc cggtatttat tgtctgctcc tctgtgccag gtgctgtgct 240
ctgggcaggg gcactgcatg ggctgcctgc cctggtggag cttgtggtct gatgggtgag 300
gctgacccaa gcccacccca ttgccaacag ggccagggca agagtacaca caggggcctc 360
ataccatatg tctaaatatt taaaaagtta tcaatcaagc taacaactgt taaataaaat 420
atgttctatt ctcctacttt gaaaaaaaaa aaaaaaaaa 459

<210> 20
<211> 555
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (48)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (50)
<223> n equals a,t,g, or c

<400> 20
agctccaccg cgttggcgcc cgctctagaa cttagtggat ccccccgncn tgccaggaat 60
tccgccacga gcaaggtcac agagctagaa aaaggcagaa ttgggaccta tacccagaat 120
ttctaactct agctctgtaa agctgggaca ctggagaagc agaggttttg gtgtagtact 180
cctctgagct cggggtctta gaagtccaca tggggctgct ggagtggtga ggggagatgg 240
aggtgggaag aagggagaag acccctattc ccctattctc tttcaatcag agaggattcc 300
tcgacttatt tacctgcctg tgatctcatc tgaagagaat tctatgaccc cccaaaatct 360
gcgattcact ctgttccagt tctgttactc tttatatctg gagctagaac tgggcttcag 420
atcactgtca caagaggtga ccagagaatg gtgcttgagt tacttctttt taataaaagt 480
ttgctggcaa gttcctgtga gtgagttcct gcttgtaaaa gagaacccat tcttacttct 540
ggagaaaaaa ctcga 555

<210> 21
<211> 665
<212> DNA
<213> Homo sapiens

<400> 21
ggcacgagaa actccagtta atgccattta ttttgcttct tgtttgctta acctccctgc 60
cttctagggg ttataatgag aagaaactaa cagacaatat tcagtgtgag atttttcaag 120
ttctttatga agaagccaca gcatcctaca aggaagaaat cgtgcatcag ctgcccagta 180
ataaaccaga agagctagaa aataatgtag atcagatctt gaaatggatt gagcagtgga 240
tcaaagatca taactcttga cttataaggc tagctactta ataatcactc ttgttgatat 300
ctctgccgac atcatagaaa ttgttcaagt gtcagtaaca ctttattaaa atcatgttgc 360
agaaccagca ggtggatagt atataggttt atgcctgtgt ttctttttctc catgagaaag 420
ctaaacatga aatataatga atatagtaat tattaaggga ttgagacaaa aactgtgatt 480
ttaatactta aattgctaaa gaataaataa atctgacaaa atgggtggat atcttttaag 540
tttattacag aaaaaaatgc agatgatctc ttaaaataaa actaaagata aagcaaaaaa 600
aaaaaaaaaa aaaactcgta ggggggggcyc cggtacccaa tcgccctatg agtgagtcgt 660

attac 665

<210> 22
<211> 777
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (274)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (278)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (295)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (676)
<223> n equals a,t,g, or c

<400> 22
ggcagagctc aggtaagarg caaaattact agaatattca ctctcactga aaatgagtaa 60
aaacctaact tagatgaaaa tccttatctt gttcattttt attcctggcc ttttggttga 120
gaagaatggg ccagaccatg tgtgtgtgtg tatgtgtgtg cgtgtgtgtg tgtgtgcgca 180
cttgggttta tttatatgag ccggtaaaat ttcgttcacc attaatttat gttaatttac 240
caacttctta aatgagaaca gtgagaattt tctncatngt taataataca ctggncagtg 300
catatatgca tcacgaagag aggatttcc cattgataat agatttccaa atacatcttc 360
ctgctttaag attttaatat atggatttat atataaaaac tagttaagtc attggaaaag 420
caaactgtca wccttctctt atttgagawc tcaactttag aaagtctatg ttctcaacta 480
cagaaaaataa tttttagacc agctaacttt cagatttctg cagtgcttat tttctcccag 540
ttgagggttg gtttttgttt gtttgtttgt ttgtttgttt ttcctgatta aaaagtaaga 600
atacggccag gcgcgatagc tcatgccttt aatcccagca ttttgggagg ccgaggaggg 660
cagatcacct gaggtncagg agttcgagac cagcctggct aacatggtga aacccagttt 720
ctactaaaaa aaaaaaaaaa aaacttcgag ggggggtccc ggtacctaat cgtccct 777

<210> 23
<211> 540
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (341)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (378)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (425)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (450)
<223> n equals a,t,g, or c

<400> 23
gaggatcccc acagggcccc tctgtagccc tggggagtcg gcagtgctgg tctaggcccc 60
ttaggagagg gggcaggggg gcagcagtag aaatgtggcg gggtccgact tggtgtttcc 120
ggccgtcttt gtgtctrtgt tgtgtatgtg gagtgtcatt cggtctttat gtccctcacg 180
gcttcagtct ctccatgtgt gtttctgccc caggctctgc ctggctgtcc cttgtgtatt 240
ccatctgtct agcccgtggt tccatgtcag amcggsttte ttctcgggam agcctggttg 300
catctggggc atctgttttg ttggtttgct tctgggtgca ngcagaccca ggagtgggtg 360
tctctgttcc ccgagcanct gtctctggtc tctggtggtg tgtgagtcca tctgcctgcc 420
tcganttggc cccaaccaag ccccccccan ccctctcttt ctctctctca atcttccctt 480
tctcttccaa ccccccaaaa tgagatggtt gagtgccgtg ggttggaggg aagcaatggt 540

<210> 24
<211> 484
<212> DNA
<213> Homo sapiens

<400> 24
ggcacgaggt ccggggaccg agggatgtga gccctggcta caactccagg acaggaggga 60
gagaatgcaa ctcagcctgt ccctctgtgc atttgtggta tgcactaacg ctgtctgcac 120
acatgcagct accaaccaag ccagactggt ggggttccta aaggtcctga ggcccgccca 180
cagccccctt tgcctctagg ttgctttccc tcccagttgc ccgcctctgg tatttgttgc 240
tacttacaga atctttagga ccaaagggct gagcgtgggg ccaagaatct ggtgagcaac 300
aagtcactgg ctctgccccc tccacttttg acagggtgta cccggggtgg ggagacggtg 360
atcctagacc cgctgtcacc tgtggggctg ttcagtgcca tgagggtaaa gaacgagttg 420
gtcccactgc tcatagttta tccctgccac ttggcacagg gcatagcaca aagcaagccc 480
tcga 484

<210> 25
<211> 707
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (562)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (570)
<223> n equals a,t,g, or c

<400> 25
gggtcgaccc acgcgtccgc dcacgcgtcc ggtttctaca acccttagga acatcagaat 60
catgtgtgtg tgggtgctta ttaaataaam sagttcctgg agctcactcc cagtgactgc 120

cagtctgatg attaggggct cagctaggac ctaggtttgc gaaagctccc agctgatctc 180
atgcagccag cctggctctg gctctggckc tgggagctgg gttgggaact agtctttggt 240
gctattctgc tgawacttca agatgggctc tttgactccg tcttgtattg tcakcacttg 300
tattcaggtc tgttcttccc ctggattgta aacccttga tgtctgggtc atctcagctc 360
atgagctgag cttwcagtgg gtgctcagtg gaacagatgc tgaatggagt caggctgtag 420
ggaggccagc gtgtgttggt aagtgagaga caaaaatcat tttaaaaaga atcttttgc 480
ccttcagttg tgtttgccat gagttaatgt gatttactct agtggaagcc agtgcagctt 540
aagtggaggt cttgccctga antggagccn ggttatggat cagcagagct gccaaaagcg 600
ttttggggga aatgtttctg tgtcaccctc agttgattga actcaagttt tcactcccgt 660
ttaacaccac gtgggggcca ttctgacttc tgcggagtgg gtatgat 707

<210> 26
<211> 793
<212> DNA
<213> Homo sapiens

<400> 26
ggcacgagta ccatttattg agctctagac atatactagg cagtgtgcta agacttgatg 60
tgtgcatgag ctcacctaaa agtctggttc tactattagc tgtaatctgt agggaagcta 120
cataacttcc tcaagctatg twtttctaac tcaaagacag gtaccttaaa gatcatctgc 180
tgctgcctct cctttgaccc actaacagag actacaggtt attaagcaat ataaaacaag 240
ggttattaac agactctgtt ttwgctgca tccccytcaa caccccgag ctccacaaat 300
cttaaagtca aatgctctta gcctacttta ttttggtaca cacctcagaa acgaacagaa 360
ctgtcaaaca cctgtgaagg caaagatcag cctgttctg ctctacacgg cctctgcagc 420
agctagcagt acttagctct cagtagcacc cactccaaca gcaagttgtt tagctgttcc 480
ttatacacac gcacacacat acgcacactc acacacacac agactctgaa gcttccctgg 540
cctctccatc taactaccac catccttacc tcttgctgca aaaactccta actgggcttc 600
ccacttcaat actttctcaa ctcaaaaagc caagtgttct ttttaaacct taaatcagaa 660
cacgccactc ttctgcttca gattccccaa ggatttctac gcacttcata tctaaactac 720
ttacgatgac ccaaggccct actagatttg gcctgcttac tttccagcgg cacgagagag 780
aactagtctc gta 793

<210> 27
<211> 638
<212> DNA
<213> Homo sapiens

<400> 27
gataagaaat tatttaaatt tctttatgaa tattgttcct caatttagcg ttcttcctca 60
ttttgcctat ttctctttta ttatcctata ttgggctgtt ttgttcagcc aaacaatttg 120
tagcatgtct gttttcaaag taaaatagtg atatatttaa agttctaaat gtgttcttta 180
tgtatttta aaggagatgg gtaaaataga atgtatttct ctttaccctg atgacattcc 240
cgtgatatat ttcaaataat atttttgatt gggtaagcca gtaggaccaa atccatggtg 300
atcacagata cagattcaca aatgcataga gagaatcata aatagatgca tatggaggag 360
tctgacagta tagtgaaatt ggtttcaagt aatttgacac attagaactt tcaggcattc 420
acctgccagt aatccttatt agaaatagga ttggaatatt ggggtcacca gctcaagacc 480
atttttttgt gagagctgaa caataaccaa aagtcagagc tataggaata aaaatgaacc 540
tattccagtc attagaactg tttctctgaa taagctcttt cttcctctcc ttcataaaaa 600
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aactcgaa 638

<210> 28
<211> 528
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (421)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (436)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (459)
<223> n equals a,t,g, or c

<400> 28
cttaaaaaat aaatactatc tttctctctg gcctctccat cctccagaca atcactgaat 60
tacaatattt gcttaacagt agattaatgt caatttttctg gaattttata tgactgatat 120
aacatgtttc ctcttttcat acctgagtac tctcctgagc cctatttatt tagatgttct 180
tctttttttct ttattattat ttttatttca catagcaggg atgcatattt tgacattcat 240
caatcatgat atatgagtag ttcattcttt ttatcttaga atatgacatg ctatggaaat 300
cactgtatac gaattcatct gcttatggat atgttattgc ttcttatttt tgtctgttag 360
gaataaaact gcttgttaag caaaaaaaaa raaaraaaaa aactcgaggg ggggcccgaa 420
ncccaattcg ccctanagtg gagtcgtatt acaaatcant ggccgtcgtt ttacaacgtc 480
gtggactggg gaaaaacctg ggcggttaac cccaacttta aatcggcc 528

<210> 29
<211> 919
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (380)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (432)
<223> n equals a,t,g, or c

<400> 29
gatcgttttt gccattgcag tgaccaacag gactgtggac ctcagtaaag gctttcccta 60
catcagcatc tgcrgatcct tccccccctca ragctgcatc ttcagccagg tgctcaatat 120
gggagctgct ctggccgcgt ggatctgcat tgtccgttac caccagctcc gggactgggg 180
cgtcagaagg tggcctaacc agctgatcct atggacgggt cttctgtgtg ccctgggcac 240
ytccgtggta ggcaatttac caggtgagac ccagtcggcg cccagggtct gtwmccggcc 300
ggcstytgga aytacaactc ccagcatgcc ccgtggccat aggcttwawg tctcgggggc 360
tggttcccgc ccgcccttcn tgggacttgt atttttctct ggccattggc ctggaccggc 420
tggatccttt gntctctgag tggggcatta cgagcgaggc tgtttgtatg taggattcgt 480
tgattccagg acgttgggat aattttctgc cagccccctc ccccagctta tttaatgatg 540
aaattactgg tccaggcgca gtggctcatg cctgtaattc cagcactttg ggaggcggag 600
gcaggcggat cgcctgaggt gaggagtttg agaccagcct ggccaaccaa catggtgaaa 660
ccccgtctct cctaaaatat gcaaaaatta gccgggcatg gtggcaggcg acttaatccc 720
agctacgtgg gaggcagagg cgggagaatc atttgaacct gggaggtgga ggttgcagtg 780
agccgagatc gagccattgc actcaaacct gggggataag agtgagactt ctctcaaaaa 840
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa actcgtaggg ggggkyccgg tacccaacgc 900

gccctatagt ggatgcgtg 919

<210> 30
<211> 864
<212> DNA
<213> Homo sapiens

<400> 30
gctcgtgccg caacatacta catttatatt aaagtgtatt tggataataa ttgccttcct 60
tgtatttgtg attgttgcct ttaagatttt aatatagaca attaatagaa ttgcttatgc 120
acattttcat aaatgggttg ttgggttttg tttattttgt tataccttgc cttgcacatt 180
tgtgtccaaa attacattta ctcatataaa atcatttgcc tgcagtcttt tcattatata 240
gtccgtaaaa tacagatatt tgtctcttaa tgaaatataa cattcctcta tcattagatt 300
agattaaatg agtgtatctt ckgtaattta taagttaawt ggatttaaca ttttgttgac 360
aaaacaccta ggcaccagca gttttgtgta gcccatagtt ttagtttgaa gtagctagaa 420
tcctctagtg tacagtttga cgagtttcat ctcacctatt taggcttttt ggtggtttga 480
tacttgacat caaaaggaaa gcacctttt tcttgagtga cttcaaggat gcattaagcc 540
tgcagtgcct ggcctcgatt cttttcctat actgtgcctg tatgtctcct gtaatcactt 600
ttggagggct gcttggagaa gctacagaag gcagaatagt gagtacaaag attggtagtg 660
gccaggcttt tagctcttca gaggcaagtg tctgtatgca tttgtctcac tattcatact 720
tttatttgaa gagtctaccc acagcatgat taacgtgacc caaagcagac tttccccaaa 780
ggtaattgct gtggaaaaca tggggaagcc atttgaacag aagatgcaca gttgaggtaa 840
aaaaaaaaaa aaaaaaactc gwag 864

<210> 31
<211> 919
<212> DNA
<213> Homo sapiens

<400> 31
ggcacgagtg atgctgctgg ctgccttcct cgccctgttt cctctccatg actccagggg 60
tttgaagcac acaggagctg gacatgtcaa ttctgtagct cttctcccaa taccactgaa 120
ggccgtgagc ctctctcctg tttccagcct gcaggtgccc tgttgctgct cttcattcca 180
gcttctcctc acttttctct cagtctcttg agcttggaag ccttactgta gcttgtgtct 240
cctccctggg cacttgaggt caggcttttg ccttttgtc acattgagcc acatgccttt 300
gatacacagt tgtagcaaag aagggaggtg atgaacttgg ctcacttctt tttctgattc 360
ccctccctac tcatcctgca ctccccaccg aaccccagat atcttatagt cctaaggctt 420
gtagaggatt aaggaaagga attggagatg ggttttactt agttcacaga aaagctttct 480
ttgggatttt tcctcccccc tagggctttt taagtctagg tgaagtgaaa gttcacacat 540
gtgtttgttt ggttgctctg taattagcta ctagttttta tccctagacc ttctctgctc 600
cagtgtcttg ttcatgtgtc ctgaccccgt gtccttgaat tcccactttg ctttgggatt 660
taagttattg tatgttgtca acaatattta aagatgaaaa agtcctgaag gaaacttacc 720
aggttctttc ctttggcttt ttttttttt tctttcgagg tactgtaaat tgttaactag 780
ggatgccaag caggcttggt tcaatggcta aacctcttat tgtattacag tgtaatgctg 840
atctcagcct ggtctcaatg ccagagcaca cagagacttg aataaaactg ttataacgat 900
taaaaaaaaa aaaaaaaaa 919

<210> 32
<211> 956
<212> DNA
<213> Homo sapiens

<400> 32
ggcattttca gtcaaaaata tggctgccgt ttaaggtgtg agctttttgc ctttttacct 60
agaaaaacaa tgatatgtaa atttcttatt ataatttgta ttactctact cttatttgct 120

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atttgtcaac tctgcaagag acaagggttg gtacagaaaa tatcatttta tcagaaggaa      180
accttgtctt ctacagtagg tactaccttc ttgagctgat tctggataat aaagcttgct      240
tcgcaataat ccagagtttt ccaaaccata tatttgactc cctttactga ctgatatgca      300
aagttgtgtt taactatatg gaaaattgtg aatccttttc ttccaagtct acacactcca      360
cttgcttttc ccttctacct tgaattcatg tgcattcccc cagttttctg cctttgtaat      420
ggaggcttca gttcttctgc agccacagtt gcaggaaacc caattgtaat cagcagctgc      480
cctgctgsta aaagctatta gtgccmatgt tgttaatgac cgacccagtt gaatgtgctg      540
atttaagggg tagacttatt tcttgtcact ccctagggcc ttgttcttaa atgagatttc      600
tacgttgttt agttgtttac tcctctagca taaggagtat taaccactaa ccaccacatt      660
cgtatatcag cacgttgaat tgaaataatg gggaggttaa gacatatcac taccttgag       720
gtatgaagac acgcgccctg aaaaaacttg gctctcaccc ctaatttttg cctaaagaag      780
ttggatacca ctgcaatttg ctctgaagtt atacatgtta ttgtcttcaa gggactatag      840
gatgagaagg gtacagttag gtttcttttc agaactaaac acattagcag taacctgcaa      900
aaatcaatac caattacttg caagcaaggg cttaaaaaaa aaaaaaaaaa actcga         956
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<210> 33
<211> 566
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (400)
<223> n equals a,t,g, or c

<400> 33

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gggttcctga gctgactagg taggtagtga gcgtgtgtgt gctggagaca ggccagctgg       60
ggcctgcagc gctctgtcgc tctgtgatgt tgacatgggt gtggtactta attatgacct      120
cagtgcttca agcctcggtt tcctcggtgg tgagagggag catattggtg ggagggagtg      180
aggactgtrg ggaggggggc tcgttgatac aggtcagtct tggctatgtg ttggctgcaa      240
gggaggacag gcaggagtgt ggaccggaca ccgtcagttg tccaccaggg atgaggctgg      300
actgagactg ctgcagcccc gctggttggc tggggtgggg cagargcagg gggccggtga      360
ggcagcctca ggaagctgct gcccctgaac tccccgggan gttccccaat ccctctccct      420
ctttgttcac tggccgggcc tccgtgtgga aagggctatt tttagccctc gctttttttg      480
gttaatgggc ttttcgcggc ttctctcttt gaaggggcta wttcaggagc agacatcart      540
gtctgcattt ggactccttg gctcga                                           566
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<210> 34
<211> 1564
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (796)
<223> n equals a,t,g, or c

<400> 34

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gaattcggca cgagattttc ctaaccattg aaagcttttg cccaagtgca cctcgtggtg       60
aggatgatga taatttatta aggacttctc gcgtgccaga catcatgcta agtgctttgt      120
ctgcattata tttaatcatc acaatattcc taaagggtag ttgctgtagt tgtcatcatt      180
gctttacaaa tgggaaactg tggcttagaa agttcatcag tggttcccaa ccctagctgc      240
ccatatttag agtcacttgg gaacctttaa aacttctcga tggcgaacta caccccagcc      300
cagttaaatc acagtctctg aggtgggttc caggcatcgg ctttttttcc agttcctcat      360
gtgcggccaa gtttgagaac cagaggtcac acaggtgcya agtgyagagc tgaccttcca      420
acccaggaag gcgggtgcca aagtcacagc tggcaaaagt caccatcagg ttattcactg      480
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ggaatttgaa attatgctgt caagctactc tacagatgta ccccctttggt ttctcaagtt      540
cttttcatcg aacttgccac agacttattt tcctcattca ggagtaaaga aatggggctc       600
ctgcttctca ttaccttgga gggattctcc cccactcacg tttatatctc ttttaagctc       660
tcatttgacg acgtttcact tatatcactt gcaccatggc atcatctgcc tagggttttc       720
tgtttatttt cacagagcat acacatcact gtgtattcta gaaacagctg taggctcgta       780
ttaacaaagt gataanaatc tggggctwtg aagacatgta ggatattagc taactgaact       840
gtgctatgag attgtttccc tttcttcttg gcaaaccatt tcagagcagc ctggtgtgga       900
gactgtgtta ctgaaatggg gccataggag cctccagact cctttctccc tgccagaggc       960
tgattaggta gatcccatag tgcagaactc catgtcacca ccacatacgt gtatggcaca      1020
cgtgggccaa tggaaagggt ccaggagttc ttactttcta actggtcatg tgtaaggaag      1080
agagcacctt cctcccttaa caccaagggt ttcaatagag accactgagc tgctacatta      1140
aatgaaagat gcattttctt gtgccctggg atgctgcccc ttattcaccc gtgtttagtt      1200
ttatcttctg tgtaaaagat actcgagttt aaatggctta aaaatgaagc aaggggctgg      1260
gcacggtgct cacgcctgta atcccagcac tttgggaaga tgaggcgggt ggatcacctg      1320
aggtcgggag ttcaagacca gcctggccaa catggcgaaa ccccatctct actaaaaata      1380
caaaaattct ctatgaatgg tggcacatgc ctgtagtctc aaatactaga gaggctgaag      1440
caggagaatt gcttgaacct gggaggtgaa ggttgcagtg agccgagatc atgctactgc      1500
actccagcct gggcaacaga gtgagactct gtctcaaaaa aaaaaaaaaa aaaaaaaaac      1560
tcga                                                                  1564
```

<210> 35
<211> 1035
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (522)
<223> n equals a,t,g, or c

<400> 35

```
gcagttttcc agcaccattc gttgaagaga ctgttctttc cctgttgaac gatcttggca       60
gccttgtcta aaaaagatta accataaatg cgagggttca cctctggact ctcaagtctg      120
ttccactgat gtgtatgact gtctttattg ttttctatta ttcttttatg agattgttat      180
tcaggtgcag ccacaatagg agacactgga gaggctcagg aaaaaacaca gtttatcaca      240
caggtcctag agacgaggca tgctgtgcca tgccatgctg ggccacttgg ggaagacgct      300
agggtggtta ggaggaggga argattaggc tactgccttc atcgaggttt ccttagggta      360
gggcagggcg aacagtttag tttgaataat tttggcatac tttagactgg cggggtggtc      420
tcgttgcctg gcacctggct ctgggatgat aggtagagga gtagtgcctc ttggggtata      480
agggccagat agaggagata tggctctgga ttttgaatag cntgscatat taaagacata      540
ctcctagctg ggcccyttgt tatctttaag aattggctag accttggagg gacagtttct      600
caaatagcta gaaaggttct ttaacatgtt aaacatcagt atacaagaaa agctaaaagt      660
ccatctgtgc cagtgccata ctgtcthgct tactgtagca gtgtggtaag ttttgaaatt      720
aggaagtgtg agccgggcgc ggtggctcac gcctgtaatc ccagcacttt gggaggctga      780
ggtgggtgga tcacgaggtc aagagatcaa gaccatcctg gccaacatgg tgaaacccca      840
tctctactaa aaatacaaaa attagctggc gtggtggcag gcatctacac tcccagctgc      900
tcgggaggct gaggtcagga gaatcacttg aacccaggag gcggagtttg cagtgagtcc      960
gagattgagc cactacactc cagcgtggcg acagagcgag atccgtctca aaaaaaaaaa     1020
aaaaaaaaac tcgta                                                      1035
```

<210> 36
<211> 620
<212> DNA
<213> Homo sapiens

<400> 36

```
acgcaggrgg ccaaggggcc tcttccaggc tctgggcacc tccagctgag gggatgtggg      60
ctgagaggag atgagtggct gcaagtggag gaagaacatt acctacttca gattttatgc      120
ctcttgctct gaaacgaggt cagcttttcc ttatcccttg gcttttcccc cagggagttt      180
gcccgttgga aggtgaacaa cttggctctg gaaaggaagg acttcttcag tttgccattg      240
cctcttgccc cagagtttat ccggaacatt cgcctccttg gaaggagacc caatctgcaa      300
caggttacag aaaatctgat taaaaagtac ggcactcatt tcttactttc tgccacccct      360
ggaggtaagc aacatcacaa tcccaagcta attggttgcc agaccattgg aaataacgtt      420
aagactcgtg tagcgtagct ccaacagtct tatcttcytc cgggcctttt attgcctgag      480
aagtctttct ggtgcatttg aaaacagtgc agtctcttca catctcaatt taccccagaa      540
catctctatt taattattcc ctgaggaggg gaagttgggt atggcggttg gaggtggaca      600
ggctcctaaa aaaaactcga                                                 620
```

<210> 37
<211> 973
<212> DNA
<213> Homo sapiens

<400> 37

```
ggggactcag tcacacagaa aatagaagaa tgtgtgtaca gttggaaggt ctcagagaaa      60
aggagtctgt tggacagaat gaccagtctg tgactactgc cattttтcat gaccatatat      120
caacccacat tacagatgta acttagtgag agaaaacatc tccctgtttt ccttcatata      180
ttatgaaata tttacttttt ctagtatttt gtctatctta cgtcaaagat ttaaatatct      240
ttgacctcct gtactaaata ccacgccaca tcagttttag ttgccтttct tttttcctta      300
ggctagtttt ttggtatacc atttctaaac caatggtagg aacattttaa ggcatctttt      360
gtctggaata wgttttagca tgtmcagcat gaaagtttta tatgtttatt aatttttgtt      420
tataattgtt aatgaatatt aattttgtta atgaatatat attaaaccaa ttaataaaca      480
gtcacaaagc tgcaaaccgk tttaataatt attaaagttt taatttttta atggattttg      540
gtcatctaag ttccgaaatg aaatacacca aacttgttct tactttgcca aattgtccta      600
ctgtttctca gaatcaacat ttttagacat tatgtagaaa cactctttaa cctagttgts      660
tcaggcttag tagagaaagg aaaagaaaga aagttggagc tggaagagga aagttggtaa      720
atgtggtcag tagtgcattt tgtgtgacca ggcaagttct gcagaacctc ttctgaacac      780
cttcacctgt gtaaaatccc aggcattagt taatctccaa ccactatggc aggatatgca      840
tctgagagca aagaggcaaa tggcaagcag agatcacaaa ggtgcaagag ctagagtagt      900
gatagaacca gtgccaggac gatctaaatt cccttgcatt gtcaatacrc aaaaaaaaaa      960
aaaaaaaact cga                                                        973
```

<210> 38
<211> 838
<212> DNA
<213> Homo sapiens

<400> 38

```
cccacgcgtc cgccctcccc tcactctctg ttctgctttc atttcttgga gtttcactag      60
atatctcata taagtggaat cataaggtat ttgtcttttt gtgattggct tatttcattt      120
agcataatgt cctcaaggtt cattcatgtt gttgcatgta atagaatttc ctttcttttt      180
aagggtgaat aatatttcat tttgtgtgtt gagaggtagg acctttaaaa tgattatgtc      240
atgagggctc tgccctcgtg aatgaattaa tgacattacc atgggagtgg gttcctgata      300
aaagaatttg gctccтttct ctcactcttg tgcatgctct cttgcccтta tgtcтtttgc      360
catgggatgt tggagcaaga agtcccttca tcagtggtga gcccatcaac cttggatttc      420
ccaacctcca gaactgtaaa taaatttctt tttaaattac ccagtctttg gtattctgtt      480
atagcaacac aaaatggact aaaacagaag attagagaga ctttcctctt tgtacagttt      540
tctcaaatgc caaggtggca taaattggaa tagtgtgtcc tgaatctcat tagagattcc      600
tcatggttgc tctatgctat gccatgtagg gagagagggg cacaaacagg tgtgcgacat      660
gccacaagtt ttcctcctcc tttcacagga atactgtctt ggttacaatg gcctaggtgc      720
tattgcttca cagctagtct ctatagtttt gtтtttтaag agatgaggtt tcactccagc      780
ctgggggaca agagtcgaga ttcgtctcaa aaaaaaaaaa aaaaaaaaaa aaaaaaaa       838
```


<210> 39
<211> 607
<212> DNA
<213> Homo sapiens

<400> 39

```
tcgacccacg cgtccgccca cgcgtccgct tctgcaagca caatggtagc aagaacgtct      60
tcagcacctt ccgaacccct gcagtgctgt tcacgggcat tgtagctttg tacatagcct      120
caggcctcac tggcttcata ggtcttgagg ttgtagccca gttgttcaac tgtatggttg      180
gactactgtt aatagcactc ctcacctggg gctacatcag gtattctggt caatatcgtg      240
agctgggcgg agctattgat tttggtgccg catatgtgtt ggagcaggct tcttctcata      300
tcggtaattc cactcaggcc actgtgaggg atgcagttgt tggaagacca tccatggata      360
aaaaagctca atagcatctt aacgtgaaga tcaaacaaga acacaacaag ccccтactga      420
tttctgggtt tctgccacgg ccacaggttc atatccagag gaatggcaga tctgagacga      480
tccaggaaga gctaaaacat ggccctgtaa taaatgagca gacctctcct gtggtttcaa      540
attattaaac acacttccat ttctcttgga aaaaaaaaaa aaaaaaaaaa aaaaaaaggg      600
cggccgc                                                               607
```

<210> 40
<211> 882
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (198)
<223> n equals a,t,g, or c

<400> 40

```
gggcgatarg gtgctgtcct tggggtgctg tgtatatggg atgatgacgc ttatcagcat      60
tatctagtcc tttccacccc gaaattcgcc ccgattaaag actgtgttgc attatcagcc      120
tgccgaccat gcccgcgggc gtgcccatgt ccacctacct gaaaatgttc gcagccagtc      180
tcctggccat gtgcgcangg gcagaagtgg tgcacaggta ctaccgaccg gacctgatga      240
gaaacaggtt gagaagagtg aagttgattt ctcaaagtca catagcttta gtgagacgat      300
ttgaggatct gaagcccaag ctttctgttt gcmaaactgg gatcacaagt ctttcggtcg      360
gagaactgga agtctgggca gagtcgagca gaggagacct gatgactgcc tagacttgtg      420
ctcagtgctg tgttggggag aactgctacg acatacctga aattccacca aagcgtggag      480
aactcaaaac ggagcтttg ggactgaaag aaagaaaaca caaacctcaa gtttctcaac      540
aggaggaact taaataacta tgccaagaat tctgtgaata atataagtct taaatatgta      600
tttcttaatt tattgcatca aactacttgt ccttaagcac ttagtctaat gctaactgca      660
agaggaggtg ctcagtggat gtttagccga tacgttgaaa tttaattacg gtttgattga      720
tatttcttga aaaccgccaa agcacatatc atcaaaccat ttcatgaata tggtttggaa      780
gatgtttagt cttgaatata atgcgaaata gaatatttgt aagtctacta tatgggttgt      840
ctttatttca tataaattaa gaaattattt aaaaaaaaaa aa                         882
```

<210> 41
<211> 959
<212> DNA
<213> Homo sapiens

<400> 41

```
ccacgcgtcc ggtatттtct aaaacaataa atttatagtg ttaatattca tagggtcaat      60
caaaatgaag cttctccttt gggcctgcat tgtatgtgtt gcтtttgcaa ggaagagacg      120
gttccccttc attggtgagg atgacaatga cgatggtcac ccacttcatc catctctgaa      180
```

tattccttat ggcatacgga atttaccacc tcctctttat tatcgcccag tgaatacagt 240
ccccagttac cctgggaata cttacactga cacagggtta ccttcgtatc cctggattct 300
aacttctcct ggattcccct atgtctatca catccgtggt tttcccttag ctactcagtt 360
gaatgttcct cctctccctc ctaggggttt cccgtttgtc cctccttcaa ggttttttc 420
agcagctgca gcacccgctg ccccacctat tgcagctgag cctgctgcag ctgcacctct 480
tacagccaca cctgtagcag ctgagcctgc tgcaaggggc cctgttgcag ctgagcctgs 540
tggcagaggc cacctgttgg agcttgagcc tgctgcagag gcacctgttg cagctgagcc 600
tgctgcagag gcacctgttg gagtggagcc agctgcagag gaaccttcac cagctgagcc 660
tgctacagcc aagcctgctg ccccagaacc tcacccttct ccctctcttg aacaggcaaa 720
tcagtgaaat tctctagaag agtaccatgg gttcatttct atactgatgc agaaataagt 780
gaaatctaca aaagttttct ttcttttcca aagactattt cattctgttg tattcagagt 840
attcatctca ctacattgat ttgtttgtgg tagtttttcc ttggacttaa tttatattga 900
aaaaacattg ataattaaat aaataaaata gataatttag accaaaaaaa aaaaaaaaa 959

<210> 42
<211> 875
<212> DNA
<213> Homo sapiens

<400> 42
ggcacgagtg ccagtgtccc gtgccctcca gtgtcaaaga tttggggcac tgcccgtcga 60
aatggaaagg ttggtgctca gcctctggag cctcacctgc agggcgtccc cagctaacac 120
ccatccacgc accacctcca ggacgagaac ccttgatgtc aaaaccaagt gcccagtgga 180
ggcggtgaag ctctcggaaa tgctgccacc tgtgtgaggc cgggtctgaa ctcgagggag 240
tcggagctca gctgtcggtt taaagagaca ctgaggggac cgggctgccg ccctcagcct 300
gcattcctgt gcgcaatcga ttccgcaatg acagcacctt actccttcct gcggcaggct 360
caccctgcc tgtgggatgt tgtgagagga acatgagcca gacaaagact tggctcaggg 420
ctccgtggaa caagccagga tgcacgggga gctgggggag cccccascct ggggcagccc 480
agcaggccgc tgaacaaaca ccccagaagc cagcactgtg gcagggtgct ggggagatgc 540
ccctctgagc cttcctcccc cctcagacct gaatgcaccc cacagttggg ggctgccccc 600
gcccactccc ctggtaatgc ataaaagggg aggggaaggt tccctggggc ttgagctccc 660
tctgtggagg tgaggagggg agattccgtt cacatcccag gaggggcaaa atgactgatg 720
tatttttatg tatctacaca gagagtgcat tttctctcca gagatgctgt ctggttaaca 780
aaggaataac ttaagaaatt gattgattat cttaataaac tgtgcaaacc caamrrraaa 840
aaaaaaaaaa aaaaaaaaaa aaaaaaaact cgtag 875

<210> 43
<211> 630
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (26)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (29)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (56)
<223> n equals a,t,g, or c

<400> 43
ccctcccttа aggggaccaa agctgnagnt ccaccgcggt ggcggccgct tagaantagt 60
ggacccccgg gctgcggaat cggcacgaga aacactgagt tcagctgccc tgtctagata 120
ttctggatta ctacagcagc cttctagcct atggttggaa cccatctgat acttttccca 180
ttcttgctta gaacaatggt gatatttctc tgcttaaaat cctcttgtgg ctcttttttg 240
cccattaata aaattcaaac tccatttatc cttaatctca tatacaaaac cttcaagatg 300
tgctccttac ctaactctct ttttcccct ttatctttca tatttttcat ttttttctt 360
acctaaccct gtagccttat ctctcttctt ggatgatctt ttgttctacc aatacccagc 420
ttctggaatg ctagtgtttg tttactcagt cctccatttc ctcttcctgg aattctagcc 480
tctcttcctt cccctaatct agtatactcc tactggtcct tcagaactca gtttaggtta 540
taattctcca aaaaattaca attaggttct ctctctggat cccatccctc aaaaaaaaaa 600
aaaaaaaact cgaggggggg gccggtaacc 630

<210> 44
<211> 571
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (460)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (494)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (562)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (566)
<223> n equals a,t,g, or c

<400> 44
gcaacatcgt ccttactcct gcatttttct gacgggcatg ctcccacgca gcttgcgcaa 60
caccaagcgg gcggtcaaac tctcggctca attgttataa gatcacataa caaaactttc 120
atcctggagc tctctcatgc gccgtttgct gctcgctttg ccgtttgccc tgctgccact 180
ggctgtcgct catgctcacg aagaccatga ccacgagcac ggcagcctcg gcgcccatga 240
acatggcgtc gggcgcctga atgccgtgct ggacggccag gccctggagc tggaactgga 300
cagcccggcc atgaacctgg tgggtttcga gcatgtagcc accagcgccg ccgacaaagc 360
caaggtcgcc gccgtgcgca aacagctgga aaatccatcg ggccctgttc aacctgccca 420
aagccgcagt tgtgtggtca gcaaccaagg aatcaacagn cgttgttcgt gacaaaccgg 480
aagccgagca tgangacgat gaccaagcct ccgacgggaa aaggcggcgg cggcccacaa 540
agcatgatca agaccaaaat gnaatncacg c 571

<210> 45
<211> 930
<212> DNA
<213> Homo sapiens

<400> 45

ggacaaaatt gacccatttt caaataatgt ttataaccag gggctgttac tgttttgttt 60
ttttttycct agctcacaat tgtaaagcag cgagaacaac cagaaatggt tttccgacag 120
ttcctggtag aagacaaagg actttacgga ggctcttctt atgtggattt cctttgttgt 180
gttcacaagg agatctgtca gctgcttaat taattgaaac ttctctgtca ttgatgttgc 240
atttccaagg agataatctc cttcttggtg cctaattttc tagatgataa taggctagtt 300
ttgatttctt gctcattttc agaataactt tccaggaaga gatggcattt agaacttcag 360
ctttggtgct caggtataaa gccaattaag gtacaattgt accataaagg gaacaatctg 420
tttctgattg cacagtttct aatttttaaa actgatgtgg tttgcatttc ataaaaggca 480
aagtttacag aaccataaac attctcaatt ttctttatgc tagacatata aattattttt 540
caaactgtat agatttgggg taaaaagttg tctcagttcc tctcccaatt gcaatgagaa 600
aaaaaagctt aatttttaca ttatacttaa ttttctaaaa ccatgtaact ccattgaaca 660
cattttcaa cttaaggtct gcatagcaga cttttaataa ccttgggatt tatctggtag 720
aacaatatgt gttctacatt tttttcataa ttatatattg tgtatgttaa aactattttc 780
cagttgtttt gtctgtaaaa ctgtctttat caatatgctt aatggttctt tgtacaattt 840
tgaaagtttc tacctgtata taatggatgt taaccagtat caataaatca ttcgtataat 900
cttaaaaaaa aaaaaaaaaa aaactcgtag 930

<210> 46
<211> 437
<212> DNA
<213> Homo sapiens

<400> 46
gcttccggac gccaacatcc gggccgcgcg gggaagggga gacgtggggt agagtgacca 60
tgacgaaatt agcgcagtgg ctttggggac tagcgatcct gggctccacc tgggtggccc 120
tgaccacggg agccttgggc ctggagctgc ccttgtcctg ccaggaagtc ctgtggccac 180
tgcccgccta cttgctggtg tccgccggct gctatgccct gggcactgtg ggctatcgtg 240
tggccacttt tcatgactgc gaggacgccg cacgcgagct gcagagccag atacaggagg 300
cccgagccga cttagcccgc aggggstgcg cttctgacag cctaacccca ttcctgtgcg 360
gacagccctt cctcccattt cccattaaag agccagttta ttttctaaaa aaaaaaaaaa 420
aaaaaaaaaa aaaaaaa 437

<210> 47
<211> 1024
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (5)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (14)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (32)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (713)
<223> n equals a,t,g, or c

<400> 47
gtggntcccc cggntggcca ggattcggca cngggcgctg gccgccttcc agctgctcaa 60
cctgactggg caacgtgggg ctcttcctgc gctcggatcc cagcatccgt ggcgtgatgc 120
tggccggccg cggtctgggc cagggctggg cttactgcta ccaatgccaa agccaggtgc 180
cgccacgcag cggacactgc tctgcctgcc gcgtctgcat cctgcgtcgg gaccaccact 240
gccgmctgct gggccgctgc gtgggcttcg gcaactaccg gcccttcctg tgcctgctgc 300
ttcatgccgc cggcgtcctg ctccacgtct ctgtgctgct gggccctgca ctgtcggccc 360
tgctgcgagc ccacacgccc ctccacatgg ctgccctcct cctgcttccc tggctcatgt 420
tgctcacagg cagagtgtct ctggcacagt ttgccttggc cttcgtgacg gacacgtgcg 480
tggcgggtgc gctgctgtgc ggggctkggc tgctcttcca tgggatgctg ctgctgcggg 540
gccagaccac atgggagtgg gctcggggcc agcactccta tgacctgggt ccctgccaca 600
acctgcaggc agccctgggg ccccgctggg ccctcgtctg gctctggccc ttcctggcct 660
ccccattgcc tggggatggg atcaccttcc agaccacagc agatgtggga canacagcct 720
cctgactcca ggaagagcca gagctgtgca gggaggaagg ggtgagaggg gggcccccac 780
acctagactc agtaaggaag tcgggttgga ccttaacatc tgcattggac aactccaccc 840
cttccttggc cttgcccctg cccgcctaca ctcctacgtg tccagggctt gggccgtgac 900
ttaggcagag gagtgcagag gagggtctgg caggggctgc tcaggccgcc tagctgcccc 960
tttgccaggt taataaagca ctgacttgtt aaaaaaaaaa aaaaaaaaaa aaagggcggc 1020
cgct 1024

<210> 48
<211> 463
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (14)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (462)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (463)
<223> n equals a,t,g, or c

<400> 48
gaattcggca cganttacag gcatgagcca ccgctcccgt ccttgactgg tgattttcta 60
ctgaaaccca gacatgttag gtattacgag actctgggtc ttactgaaac cttgcttccc 120
acgctgctac tccagcacag gaggggaggt gctgccgcgt tgctgtgagg tggaggcgga 180
agtccaggtt ccccactcag cacccatgga ctctagagaa gggggcactg tgccttactt 240
tggagggtgt gggagtccta gattctacta gaccagcact ggctgtgcgg ggtgggggtg 300
tcaccttact gctctttcat ggcctccact ttcaccatat tctcaggatg gcagtgacct 360
tggagtggag agaggggatg tgattgggca ggagacgcag gaggcttcaa aaaaaaaaaa 420
aaaaaaaaaa aaaaaaactc ggggggggccc cggaaccaat tnn 463

<210> 49
<211> 885
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (233)
<223> n equals a,t,g, or c

<400> 49
aattcggcac gagagggctg catccttgcg ttctgtgagc tctgcccgtt gggagcatcc 60
atgctgatgt gcaggggccg tgcagcactg cattcttctt gccttctctg ttctgtttag 120
tacaaccacc ccagcaggtc tccagttcct gccaggttag tgtggatggc ccagcaccat 180
ctcctctcca tcttgttggc tatcctctct tgttcctcac aaccccgcca ggntcgcggc 240
tcaggagctc tgccgtgtga agtgtgctca gcagttctcc tcacatgtct acgcaaaatc 300
tctggctccc tgtgtgtctg agcccaacag acacactgag cacaggagtt ggctctcagc 360
tcctcccagc ttgccgtgac tgagccytgc cgtcctgtgg camcgccasg gagaccacag 420
tgtccaactg tccaaccttt acgtaattgg catcccagga ggagaagcaa gagtgaatgg 480
ggcaggaaaa gatcattaaa gaaatcgtgg ctgacataaa aaaggatgag ttcatgtcct 540
ttgtagggac gcgtggatga agctggaaac catcattctg agcaaactat cgcaaggaca 600
gaaaaccaaa caccatgtgt tctcactcat aggtgggaat tgaacaatga gatcacttgg 660
acacagggtg gggaacatca cacaccgggg cctgtcgtgg ggtgaggggg atggggcagg 720
gatagcatta ggagatatac ctaatgtaaa tgacgagtta atgggtgtca gcacaccaac 780
atggcacatg tatacatatg taacaaacct gcatgttgtg cacatgtacc ccagaactta 840
aagtataata aattaaaatt aaaaaaaaaa aaaaaaaact cgtag 885

<210> 50
<211> 847
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (337)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (407)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (415)
<223> n equals a,t,g, or c

<400> 50
ggcacgagtg aaaccataaa gaaaaccaag ggggtgataa atataaaatc caacgtggtt 60
attacctggt tacgggcagg actatgatag ggaagtcact ggttatgttc tgtttcctaa 120
gctgggggcc aggggtacat gggtgtgcac tttattataa tgcttccaac cgtataggta 180
tattttatat attctgtttt acatatttga gattgcatga atgtgtaatg ctcagtaact 240
taagagtaaa tgaactgtga agaattagag atggagtttt gagggatttt ttgttttggt 300
ttgatttttg gagaccagat cctggctttg ccgtcangct gggaatgcag tgatgttatc 360
catggcctca cttcagcctt taccctcctg gggctcaggt gatcctncca acttncgggc 420
ttcgattagc tggggactcc aggtgcacac caccacaccc agttgacttt taaatttttc 480
gtggagatga gttctccctg tgtattgccc cacgctggtc tcaaattcct ggcttatgga 540
atcctccctg agccaggtgc ctggccagtt tttgggttgt tttgtttttc ttttttgaga 600
tggcaatttc gctttattgc ctcaggctgg agtgcagtgg cgcgatctcg gctcactgca 660
acctccatct cccaggtaca agcgattctc ctgcctcagc tactggggaa gctgaggcag 720
gagaatcact tgaacccagg aggcggaggt tgcagtgagc caagatcacg ccactggact 780
ccagtcctga gcaacagagc caagactccg tctcaaaaaa gaaaaagaaa aaaaaaaaaa 840

aaaaaaa 847

<210> 51
<211> 580
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (557)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (569)
<223> n equals a,t,g, or c

<400> 51
caagaaagtt tgcatttata acacaagtaa cacatgttaa gtcctctttc acaatctctg 60
ttagttgcac tcaatgttct ttttctcctc ccaaacttct tagcactttc taaaaacctg 120
acctacgatt gttattttag gttcttccca actttttttc tgcctcccaa ggaaatgtgg 180
tatctctgac ttccacagct ctcactttga ttcataacac caaggcttct tccccctgga 240
gtgggagaca caatagggat ggggatgtgg gcagaagaag aggattctat gaatatccat 300
agttttattt cacccacccc aaatgtattt atattaaagg acccactgaa gagcgctggt 360
gagatggtag actcttgtct gaagtcctta tgctacacca atataatctt cttcttaggc 420
cttctcccac taggtgaaag gggataagct tcgggacatc tagaaagggg cattaatttc 480
cccaatccta tgagctacat ttgagactca cagtattaga aagccggggc tttatcacag 540
tctctttgga agaagcnaaa tttttttcng gacagctttc 580

<210> 52
<211> 598
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (515)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (523)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (558)
<223> n equals a,t,g, or c

<400> 52
ggcacgaggg tcggcgggca gggcggggct gcatgcgatg acgtcgatgt gtccggccgc 60
ggcgctggcc tggccgacct cggcgatttc cttgatcgtc agcctggcgc ccagctgggc 120
cgcggcgcgc gacaactggg ccgcgtcgcc atacaccacg caggcgcgcc cagccctgcg 180
cgcagccttg acgacgattt cggggccgat gccggcggca tcgcccatgg tgatgcccac 240
gggcagggag gggttcacgg tgctgggaat gggattgcgt tgcggataat gctacacccg 300
ttcgcgggcg acggccgggc ttactgcttg ccgtttttcg gcggttcgat gacgccgcat 360

tcgaaggtga ccgtggcgcg cttgggagcc caagccggtg gcgttgtttg gagtgatctc 420
cggcttgaag cagcttgcgt tcccatggat ttcgcaatgc tgcttcgcgc gcttgcaacg 480
cctgggttct tcagcttcca acccaagttc agcancttgg ctncccggaa gcttttaagt 540
ttaacctggt aaagtgtncc cttgttcgaa ccttggcttg aaccttcggc ttcaatgc 598

<210> 53
<211> 571
<212> DNA
<213> Homo sapiens

<400> 53
gaattcggca cgagtcccac cagcccccca aaaaacctct cagtagtttc tttcagtgta 60
caaaatgatg agcatttttc tatgatgagg ttttaaccat tattcagggt ggtcttttgt 120
ttttaaatct ttttttaact aataagattt acggtgtgta ttttatacag aaatgcatta 180
taaatgtttt taattgtgtt ctgttttttg cagtctttaa gtgccatgcc aattgttctt 240
atattctata gaagttcgct caaaatactc aacaggggaa taggcagcgg acagtcagaa 300
tggttggaat tttggctttc taagaaaaac tttatttttgc ataagcatgc ggtcagatca 360
ttttgtgcat atgcagcctg gattggatgt taagtaaatg cttgttcagt gccggtacat 420
ttacttaaat ctgtttttat ttttgtcatg tagaatacta ctgtggtcat cataatgtaa 480
tctatttctg tacctttttt ttttttttt actttgaagt cttaaataaa atgtataata 540
cccaaaaaaa aaaaaaaaaa aaaaaaaaaa a 571

<210> 54
<211> 1247
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (2)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (9)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (1131)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (1202)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (1209)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (1226)
<223> n equals a,t,g, or c

<400> 54
cncccacanc cacaaattgg tttggttggt tgtaagtcag gcttcccacc aaagtccaat 60
atttctaaca ctctagtgca ataaaaatta ttattaaata gctaagaggt gtgcatgtgg 120
gaaaggtcag tgcatatccc tttaggaggg gagaatgttg taatatatca gctatcgagt 180
tgtttaaaaa aagtgtatyc aaycgtatat tgtctatagt atgtgctatg aaatttgcat 240
ttatgatatg taacaggggc aaagccaaat tcatgttact ctgttcagtc agaaacattt 300
tgtggcatac agcattcctg ggaagtgctg tactttgttt cgttttggtt ttagttttgc 360
atttagagtg ccttataatt gatgcctatt ttaatagcat ttctttttag cttttggttc 420
gtatttccat tcactgttcg tatctgttac tttctattaa agcattatct gtttaccaca 480
tgtacaaaaa ctctttgaat aatatgcatt cctagttttc agccaagtcg gggatgttag 540
tgattgtacc agcccmaagc acttggataa tcagggccct tcttcctttt ataatcaatc 600
atcaacatca gaaaaagcta cttgttttat ttatattccc ttccaaatcc gctctggaac 660
atgcagtaac tgcaccaaac ttatttagt aacaaatatc attggcaact ttggaatata 720
tttgatattc cattaggatt tttctaaaag gggaaataaa ctatatatat atatgtatct 780
tacccccaat tcttccaaca gaatttctat aggaagccat ggatgatggc ataagtttgc 840
cacatattac atgattttaa ataatcctca aaatacccaa ggaactctta aagagttttg 900
gtatgagtat actactttgg tttaatttta gcttcatgga tgttctgcat ggaaggattt 960
ttgttttcca cattttccca ttgctagcag agtgaaatcc aagagaccaa acatttgcaa 1020
gcattgtatt tgagcacttt tgtaaaaaac aaagaaaaaa aaaaaaagga aaatatatat 1080
aatacttaaa aaaaaggtat ctaggaaggg ctaccctcag gattggggac ntctcttaac 1140
cctacctccg ggaccccggg ggagggatgt tgcccctatg tgggggtctg tttattccat 1200
tnttttcnt tttagggttg gtatcntttt tgggggggttt ttttccc 1247

<210> 55
<211> 848
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (8)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (15)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (98)
<223> n equals a,t,g, or c

<400> 55
cccccaanga acagnttttg gtaaatccaa aaattatgcc acttttaaaa aaaaaaaaca 60
aaccttaaaa cagggatctt aataccctcc ccttgttntc cccttgcttt actcctccac 120
tttagaatat tttccttaaa aatcacctca aaggactgtg aggaaaggct gtggtacctg 180
accttgttga aatcaaggcc cggcactgta ctacaggcct gtttacagat tattacggtg 240
aactgaatgg gtaccgaggc ttcaccaaag aggtactttt ttgttgttgt tgttgtttta 300
ggaataattg taccaatttt aagagcattc cccccacctg tccccacaca cccaaacaaa 360
atgtggtggt gttgccttca aaaaagagaa gttttgtgtc attaacatga cagaagaact 420
ttttaaaaaa aaataactgt caactattct atttgcattt aggagactgt tmatctatgc 480
tagattgtca ttttcccctcc ttctcccaca gaagtttact ggtagtccat gtcatggctc 540
gtagctatcc ctctaaccat accatggaaa tgcaggcacc caatgtgaaa aggagcactt 600
gctgggcatc actgacaccg ctcatgtttt acacatagtt gagtaatcag catatctaga 660
attatcttgc attgcctaaa tcatatgtat atagtgaatg ttatataata tacctggcag 720

```
gtctgtttta atttaattga ataaagatac aaatactttg tttggctggc atatattaaa      780
ttattatatg aaraaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaggg      840
cggccgct                                                               848
```

<210> 56
<211> 669
<212> DNA
<213> Homo sapiens

<400> 56

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cagcctcatt ttctcagtgc cccagaggtc taggatagga tttctaaact ggaatcatcc       60
ttaatcacct tgaagatccc ttaagaggca tttgactggt gctgccgtct gtgtcctcaa      120
agcaatgctg gtggcatcgt cctgtgtaca catgcagagc taatacccaa actaaaaact      180
gggtaactgg ccctgaagtg cttcccaatc agtaagccac agggaaatgt ttgatttta       240
tgttctgttg gattttggtt tgcttggcat atctaaaggt gcctttactt ttctttttt       300
ttttttttct ttctgctttg ttttgtagga cttgttctaa catggaaaac aagtccagaa      360
gactctcctc tgactgttac ctttgcccca agccacccca aacttttatg ctcatgtttt      420
attaaagcag gtgctccctg gaatctctgg gacatttttg aggcatttga agcagaatat      480
agagtggtct catctccttc cttaatcttc ctggtggttg ggatgttcca cttgtatcat      540
agatttttt attacagata tgctccactg tttttaaatg tgaacttgtg cgcaaatgtg      600
cagattcaat gttcttgtta cagattgaat aaatttttac tttgaarawr aaaaaaaaaa      660
aaactcgag                                                              669
```

<210> 57
<211> 680
<212> DNA
<213> Homo sapiens

<400> 57

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gttccatgtg gcactgacta ctccagagtc cctgggaaca ttatgctttt tttgcacact       60
cgtctccatt ttccacgcta tacgctcctt atatgcaagg tactcttagt agttgcagca      120
tctgtccacc gtccttggct ccgtagtatc accgggtgct tctttactaa atgagagtat      180
tcctcagttg tgggagtcga gagagagaag agggagacag agagagagag agagttgggg      240
tgcttatttt aactctggtt ctaatcatgc tgcaggtcag cttgccaaga aacacttaag      300
gctctgtttt ctgcatgtag gcaggtaatc cctgataga gaaacataga gttatcccat       360
caaaatgtga gcacagaaat gtatcaacaa catgccataa gccagtcgat atatctaaaa      420
gccaaactgc aaaccggtcc ctgtgccccc gaaagggtgt cagaatatag ttgtttttgc      480
aggttttaac attaattggc actagacaca cccagctgaa gcaaggtctg tcgctggttt      540
tgagcttcct ctgccttta ctgatgctaa aatgtttaac tttggctttg gtagatttta       600
atgcagacca agagtgctat ttttatgtat aaaatttat atttataaaa caaaaagtac       660
ctaaaaaaaa aaaaaaaaaa                                                  680
```

<210> 58
<211> 524
<212> DNA
<213> Homo sapiens

<400> 58

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gggtccatat tctccggatg agtgcatctc tttgcctgtt tacacaagtg ctgaaaggga       60
tcgtgtggtt accaatattg atgttccatg tgggggcaac caagaccagt ggattcagtg      120
tggagcagct ctattcctaa aaaatcagta gaatctaatg acaacaaaag ccatcttcac      180
aaaagggaac attgattctt taagctttaa atcaaacatg tggtcagtct acatttgaaa      240
tgttagttca aaatattaac atatagttat gttgttgatg tcactgaaat tttaatgtgt      300
aaaagcagca ctgtgcatct tttaaagtaa taaattaatg gagttattgt taaaacagag      360
tattcttttg acaacattaa atatttctgt gagaaagttc acttttccag tggctcaaaa      420
```



```
atttgtttta ggtccagaga ttttaagtgg tatattaacc aataataaat attttggctg      480
tcaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaagggcgg ccgc                        524
```

<210> 59
<211> 427
<212> DNA
<213> Homo sapiens

<400> 59

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ggcacgaggt catttcagcc ttatgaattg cccagaataa gctagatcac ctttaaggcc       60
atgtggttag ggaaacttgg gcacagaatt tacattttca acttggtgat aagatgggtt      120
taaggtaaga atcaaatagg agaaagcctt agctgttcca gcggcccatg tttaaaagaa      180
tgtgcttctt tttccaagta tttctgccgc ttgcatgcac tgagcttctt tggaaaggag      240
caccatgcag gcatattttc cagacaggac cggatttgct cgttactcag aggtgtgtgc      300
attctttgct tttaggatat ttaattagca tcttttaata gtgatattac ggtgtcttaa      360
aagtttatgc atttgaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa      420
aaaaaaa                                                                427
```

<210> 60
<211> 1263
<212> DNA
<213> Homo sapiens

<400> 60

```
ggcacgagcc ccttccggca aaacggcagc agtagcagag gcagcttctg agagcctggg       60
caggcagcag ctggctgacc aagtccactg gaagagaagg cttgtgccag ccgggagaag      120
gaagccgggg acaggatgaa agcaacaaca cctttgcaga cagtcgaccg gcccaaggac      180
tggtacaaga cgatgtttaa gcaaattcac atggtgcaca agccggatga tgacacagac      240
atgtataata ctccttatac atacaatgca ggtctgtaca acccacccta cagtgctcag      300
tcacaccctg ctgcaaagac ccaaacctac agacctcttt ccaaaagcca ctccgacaac      360
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gtcccgccgc ttcgaccaag agatcggtct tcaacagaaa agcatgactg ggatcctcca      480
gacagaaaag tggacacaag aaaatttcgg tctgagccaa ggagtatttt tgaatatgaa      540
cctggcaagt catcaattct tcagcatgaa agaccagtta ccaagcctca agcttcctga      600
ttgattgtca ttctaatgga tcaagattat atttcacttt gaggattttt tccaattatt      660
taattatatg caaacaaaaa tatctataca cttaagaaga accacttgcc tcctcgaagc      720
gcaggttcac acataggtct tcccttggcc ttctttgggt tttggattcc ccaatactcc      780
cttgcatgtc ctttgcttcc cctcagaaat cagtgtcctc aggatttttct ttgaaactcc      840
acagttcctc tgcatctcct tccaagccta cttctaggaa aacatttgga atcaattgca      900
atttactctc aatttttggt ttaaaagaat tttaggtgtc agtgaacagg aaaaagagag      960
ttttcttttgt ggagctcctt caagagtctc caagaaatca cactcatatt aatccaaggc     1020
cagccctgtg gtttaattgg aaactctagc cttgccacac ccaacatgag tgtccttgat     1080
tgagtctttg aaaccctgtg tttgcggttg tgttctggag aagcatgttc aaaaccttat     1140
catcagataa ttcatacatg atatttgtct aagccttctt acccttttctt taaataactc     1200
atatctttta gagtaacagg actacaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa     1260
aaa                                                                   1263
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<210> 61
<211> 720
<212> DNA
<213> Homo sapiens

<400> 61

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ggcacgagat ttctcacaat gacaaattct caaatattgc taatagtact gtggattttc       60
ctacattggt aaattgaagg aattgctaaa tgctgaattc agcaaccagt ttgagattgt      120
```

tgaaaataaa gattgtttct ttttcaatgc aagttcacag atcactggag ttctagctac 180
agtttgttct agaccagagg ttgcagatat ttttgtccta taaagagaca catggttaat 240
atttttggct ttgtgagttg tatagttttc gttgtagctg ttcagctctg ctacatgaag 300
caaccataga ccatacctta acaagtggtc acttttgagt accaataaaa ctttatttag 360
aaataacaga gggctggatt tggtcctagt ttgctgaacc cttttctaga tgaaggctcc 420
tcttgccaag actggctccc taccttggct gacaaattct cactttggga cttagtcatt 480
gttgctgctc tctgttattt tgcatgtctt ttctcatgtt taggtgctgt gtcttaatac 540
ttttttctta catttaattt aacaatcatt actgagcgct ggtatgtcta gtttcttttc 600
tcttctttcc tccttttctt ttcttttttt ctttttcttt atttgaaggc tctcactctg 660
tcactccagc ctgggtggca gaccaggacc ctgtctctaa aaaaaaaaaa aaaaaaaaaa 720

<210> 62
<211> 589
<212> DNA
<213> Homo sapiens

<400> 62
ggcacgagcc ccgcgcatgg ggaggtaggc tcggaccggc ccgcggagct gctgcagtcc 60
ttcgcgccct cctcgccctc cccaccgaca tcatgctcca gttcctgctt ggatttacac 120
tgggcaacgt ggttggaatg tatctggctc agaactatga tataccaaac ctggctaaaa 180
aacttgaaga aattaaaaag gacttggatg ccaagaagaa acccccctagt gcatgagact 240
gcctccagca ctgccttcag gatatactga ttctactgct cttgagggcc tcgtttacta 300
tctgaaccaa aagcttttgt tttcgtctcc agcctcagca cttctcttct ttgctagacc 360
ctgtgttttt tgctttaaag caagcaaaat ggggccccaa tttgagaact acccgacatt 420
tccaacatac tcacctcttc ccataatccc tttccaactg catgggaggt tctaagactg 480
gaattatggt gctagattag taaacatgac ttttaaaaaa aaaaaaaaaa aaaaaaaaaa 540
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaag ggcggccgc 589

<210> 63
<211> 686
<212> DNA
<213> Homo sapiens

<400> 63
tcgacccacg cgtccgaact gccaaaagct ggtgattctg ggacaggcct tcactttgga 60
gccacgggat ggggtggggg agccccatgg gcctgggaag gagggtgctg tggagggggc 120
tgcagggctg accagcaggc agcctcatct ggtcgggggc gggggcggca ggagcagaag 180
cggggtctcc gtccttggga ctgtcctggt tggccacggg ccctgaggat gcacggtgcc 240
tggggctcct gtgccggtgg gcgggggggca tgctggcctc tgagcgatca ggcgaggcca 300
gcgagggtgt gcttgcaaat tcaagcaata agaggggggt tcctgggggc ttccagccca 360
ggctagaagc ccccatggct tctggcagct ggacatcagc cccaggtatt ggggtgattt 420
tggtcatgac agtgtgcctg tcccactgtt acacgcatga atgggggtta tggggtgggg 480
gtgggactca aggcttgacc gactcctagt ggacctgatg tgaaattcct gtcaaacaaa 540
caccactttt caatggtttg ctaggagtat ttctgtattg aaagtttcta attatgcttt 600
ttaaaaaaat actaaaaata aaggttcaag ctgccaaaaa aaaaaaaaaa aaaaaaaaaa 660
aaaaaaaaaa aaaaaaaaaa aaaaaa 686

<210> 64
<211> 452
<212> DNA
<213> Homo sapiens

<400> 64
attgtgtagc attcaaaacc tgctgaacac tcaccctcaa tgtatattct ctgttctggc 60
ctgcttcaag gtcagttaca ctacttcctg ggatgggcct ttctctggct taagcttggt 120

tgtccctggc tttcccaagg atcacagccc aaaaggcaca gtggggaaaa tttatggcct 180
attcgagaag agtgagcagc ctaatcaagc caagccttga tttggggttc tcacttcact 240
ggtatttttcc ctctgtccct aattgggttt tctatagtta ctagttttcc aggccctcaa 300
gggagattct gaggcttgat gtgttctgac tgtgtcttgg ctttgtgatg ctgagtgcca 360
gaaatactct gtactataaa aactaccatc gttctttgaa acaacaaaga ggaataaaga 420
acttaattct ggtgaaaaaa aaaaaaaaaa aa 452

<210> 65
<211> 370
<212> DNA
<213> Homo sapiens

<400> 65
ggcacgagtt gcggtgaacc agaattataa cagtgagctc atctgactgt tttaggatgt 60
acagcctagt gttaacattc ttggtatctt tttgtgcctt atctaaaaca tttctcgatc 120
actggtttca gatgttcatt tattatattc ttttcaaaga ttcagagatt ggcttttgtc 180
atccactatt gtatgttttg tttcattgac ctctagtgat accttgatct ttcccacttt 240
ctgttttcgg attggagaag atgtaccttt tttgtcaact cttacttta tcagatgatc 300
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<210> 66
<211> 987
<212> DNA
<213> Homo sapiens

<400> 66
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aggcatccaa aggagcacac atgccatcga ggaagccacc acagaatcag caaatggaat 660
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ttaattctta atttacctga aaatattctt gaaatttcag aaaatatgtt ctatgtagag 840
aatcccaact tttaaaaaca ataattcaat ggataaatct gtctttgaaa tataacatta 900
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<210> 67
<211> 1018
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (1014)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (1015)
<223> n equals a,t,g, or c

<400> 67
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ccgaagccgg gctcggggcg ctgccgcggc gggcgctcgc ccagtacttg ctcttcctgc 120
ggctctaccc ggtgctcacc aaggcggcca ccagtggcat tttgtcagca cttgggaact 180
tcctggccca gatgattgag aagaagcgga aaaaagaaaa ctctagaagt ctggatgtcg 240
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tctacttctt catggaacat tggatccctc ctgaggtccc cctggcaggg ctcaggaggc 360
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tccctctgaa gttccgggtg ctcttcgcca acctggcagc tctgttctgg tatgcctacc 600
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aaaaaaaaaa actcgagggg gggcccgtac ccaatcgccc tgatgatgat ctgnncac 1018

<210> 68
<211> 762
<212> DNA
<213> Homo sapiens

<400> 68
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tggcaggaat gcctacataa cagggaaaaa tctattgatg caagcacggt ggttccatat 180
tcttgggatg atgatgttca tctggtcatc tgcccatcag tataagtgcc catgttattc 240
gcggcaatct caggaaaaat aaagcaggag tggtcattca ctgtaaccac aggatcccat 300
ttggagactg gtttgaatat gtttcttccc ctaactactt agcagagctg atgatctacg 360
tttccatggc cgtcaccttt gggttccaca acttaacttg gtggctagtg gtgacaaatg 420
tcttctttaa tcaggccctg tctgcctttc tcagccacca attctacaaa agcaaatttg 480
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aataaatact aatggcagaa aaaaaaaaaa aaaaaaaaaa aa 762

<210> 69
<211> 630
<212> DNA
<213> Homo sapiens

<400> 69
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ctgttctgca ctgtgggctg gctctctgcc ccaaccctgg gcactggccc ctggctgggc 240
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gggtcttgct aatggaaagt agcatatatg tgctttaaaa atattaatcc ttttgaaaag 360

aactgagaag araaatgtat aattttatcc catttttaat attttggtct agcaacttgt 420
gatacataga tgacaatttt gtgagttttt caaatgtgtg tacagatttt tgtaaatatg 480
actcttttgt aattaactca tgtacagcct catcctgtat agtttaatga tgaatgtgca 540
ggggacctgt ctcaggctcc tatatggtta aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 600
aaaaaaaggg cggccgctct agaggatccc 630

<210> 70
<211> 940
<212> DNA
<213> Homo sapiens

<400> 70
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tctggagcct ggaagagact cctgcccttc aagggctttg tgaaattgcc cagccttaag 180
tgtagagtct agtttttaga ctaatttttt ttgtattttt gtatttgtaa tttttgtggg 240
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caagcggggt gagggcagga ggcacaggaa gggaggagaa ggaagcctag ctgactcctc 780
ccacccccaa gggctgcccc tccctacact cctgtttgag taagagtggc agccacctgc 840
cctgtccccg ggggtgacaa ccttgagctg ggagggcgag ccccctcagtg ccttctttta 900
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<210> 71
<211> 1103
<212> DNA
<213> Homo sapiens

<400> 71
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ctgatcatcc cattgtactg caaaaaccag aaaacaacca aagttttaag tagcatttta 180
agaacagatg aatttaagtt tggacatctg caaatgaggt ggatctagca acaataactg 240
taatggactg tgacaattca atttattctt aattttgatg gttggctatt tgacttctct 300
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ggaggtttcc tgcataaatt gggaagtaac actggaaagt aggaatttgg ttagtgaagt 420
gggaagactg tatatttata atttgcatac tacttgcaat tttttgtttt tcatcacttg 480
taataatgga atggaaatgt aagctgtaaa gactctcaaa tataaaatat ttgctacagt 540
gtatatatgg tacataattg cttgttgctt ttaaagttcc ttctgttgtt ctgcttccca 600
ctgatttcat accagctcat gaatggatca ttacagtctc tccagaggct tagaatgatt 660
cagaatgttc aatgcatagt tctcaataaa caggaggcag aatttttaat gggtatttct 720
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tcctagaaat tttatacatt aaatctcctg caatttgtca ctctggatgt tactgtttaa 1080
aaaaaaaaaa aaaaaactcg tag 1103

<210> 72
<211> 899
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (20)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (85)
<223> n equals a,t,g, or c

<400> 72
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aagttgtctg gccccattag ccagnaacca gggaaatgta gctgcaggaa aatcacctcg 120
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ccacgcaatt cagttaagtg gcacttttca gagaaactgt cttggtgatc atttgggctg 240
ctgtgggcac gaggttgagg agagaaggga gtgagagctt ctactgagtt tagttggttt 300
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tttccctacc agccaagctg ttgaagctgc tgagcccgga atgatgttat cactgaggca 420
gatgacaaac cctctagttg ctagaaacca aactgctccc cgagctggtg tttccgtttt 480
ttgtactgac tgcttatttg ggcttgatat ataatggtga aaacaggaac tgtttatttt 540
aggtgataag aaaccaacat tatgacaaga agatgtcatc ttagttactc tgttaccagt 600
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agccccaagc taggttttat atccccattt tatggatggg ggaactgagg ccaataactt 720
catataactt atccaaggcc acaaaactag taataaacag agtgaaattc aacccaaaaa 780
caaactacaa atccaaattt ctttacctct atgctgtctg tacttgctgt tactagcaaa 840
gttctcttgg tgggagttac cccatcccct ctcccaaaaaa aaaaaaaaaa aactcgtag 899

<210> 73
<211> 549
<212> DNA
<213> Homo sapiens

<400> 73
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ctatcaatgc agcaattgga gtcactacgt caccggtgct gccttctctg atccagcttc 120
ttggaagaaa ttttattttg tttatcatct ttggcaccat ggaagaaatg cagaacaaag 180
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ggattccctt atatccactg gggatgtttg gcggaagctg tctcagtgat tcagtccatt 360
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gttagatttt ccttttttct tcagatttat cttataatga tattttagg gttatacata 480
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aaaaaaaaa 549

<210> 74
<211> 590
<212> DNA
<213> Homo sapiens

<400> 74
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gttcccaccc tgttctgccc caggattgtg ctggaagtgc tggttgtgct ccgaagcatc 120
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aagtggaatg aaactatcaa tcttacrcat acagctttgt tgaaaatgtg gacttttagt 480
gagaagaaac aaatgttaat acatttagcc aagaaatcca caagtaaagt actcttatga 540
aaacttgtaa aaaaaaaraa ararrraaaa aaaaamctcg agggggggcc 590

<210> 75
<211> 1056
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (1051)
<223> n equals a,t,g, or c

<400> 75
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ctgccttttt tcatctctga atccccacca ttggcctaca ttgggagtgg ggcgacctgt 120
gatgctgacg ttagaggaca aggacatgaa gggattctcc tgggccatag tcccagcctt 180
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caaatgctgg aagcctcgac ccttatccat ttacatcatc ctcggccggg ttttcctgct 360
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<210> 76
<211> 930
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (919)
<223> n equals a,t,g, or c

<400> 76
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gagccacttg gcctccaccc tccgctattg catgacagtc agcggcacag tggttctggt 120
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caaggccagc atcccagggc caccttcgat gggacccctа tcacctctcc agagacctgt 360
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<210> 77
<211> 4463
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (3308)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (3469)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (4119)
<223> n equals a,t,g, or c

<400> 77
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cataaaggca gaattcttac aagttttttt ttttaatgtg aacatagatg cagcaccgac 4260
tttttaaact tgaaaaaact ggtataatgt taacttttaa aaataacatt tggacacact 4320
agtaattgat ttttgtttac agattgtttt gtttacaaat tgttagtctt tgtttctatg 4380
agatactttt agtgtgactt tttaaatgtc ttagaaatta aaagttgtac aaaaagtgat 4440
ttcaaaaaaa aaaaaaaaaa aaa 4463

<210> 78
<211> 791
<212> DNA
<213> Homo sapiens

<400> 78
cccacgcgtc cggttctcct gcttgccatc aatggagtga cagagtgttt cacatttgct 60
gccatgagca aagaggaggt cgacaggtac aattttgtga tgctggccct gtcctcctca 120
ttcctggtgt tatcctatct cttgacccgt tggtgtggca gcgtgggctt catcttggcc 180
aactgcttta acatgggcat tcggatcacg cagagccttt gcttcatcca ccgctactac 240
cgaagagccc ccacaggccc ctggctggcc tgcacctatc gccagtcctg ctcgggacat 300
ttgccctcag tggtggggtt actgctgttt cggaggtatt cctctgctgt gagcagggct 360
ggccagccag actggcacac attgctgtgg gggccttctg tctgggagca actctcggga 420
cagcattcct cacagagacc aagctgatcc atttcctcag gactcagtta ggtgtgccca 480
gacgcactga caaaatgacg tgacttcagg gaagcctgga cacccgaggc acctggacca 540
gctatgggta gttctgtggg tggaacacat tctgtgtaag agccccactg agggctctgc 600
agcggagtga cagcaacccc agagatgagg caccagagag tgccactgca tgagacacct 660
gtgaccattc gaagtctgaa atgcgggggg ggagtttcat ttttaagtga agaccaaaag 720
ccctttaaaa ataatagttt tttatcattt tatagtaaaa aaaaaaaaaa aaaaaaaaaa 780
agggcggccg c 791

<210> 79
<211> 1292
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (488)
<223> n equals a,t,g, or c

<400> 79
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aaaaaatgag gagagaagtt acaataggga ggtcatcttc aatctgtttg gaccagcaag 120
taaaagcagg aaatgctgtc caccaccaat ggcttaaata tgtgtgttgg atggtggtgg 180
tggttggtgg ttctgggggtt ggggatgggg ggaaccttgg gatgtgatgg ttttcttagt 240
cagagatggt gctttacagc tgggaagtat cttgaacttg gtggaggtct atccagacat 300
caggcagatt tcatattttc acagacaaag gctacgttta cgtctaaggg gaaaacacaa 360
aatactaaga tagaaacctc catgcccccct caccttttca gacaacaaga acccccaggg 420
cagagggtct tcctcactct cagagttact ttgacttctc atctggtttc gtgtgggtaa 480
tgcatttnca ctcttgagtt tcttttcttt ttaaggtatt ttcattatga cgtttgttct 540
tttgcaaaga gctaattctg cagaattcta cccagggagg gccgagggaa gttagtgaag 600
gtaacgatac cagttagaaa gttgagtttg ggtcatctca ggggcctcct ttggcctcct 660
ttggcttatg ttctagagat ggcccttact tcccaggaat agatagtgat gtcttactga 720
gttgcaggta gagtctgtat tgaagcgcaa gattttcttc cctgacttgt ctgggaatcc 780
ttacccagga ctgtggcttt cctcttccat atccctccac caggargcag gctctaagcc 840
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accaacatgg agaaaccccg tctctactaa aagtacaaaa ttagctggca tggtggcaca 1140
tgcctgtagt ctgagctact cgggaggctg aggcaggaga atcgcttgaa ccttgggggt 1200
ggaggttgca gtgagttgag atcttgccat tgcactccag cctgggcaac aagagtgaaa 1260
cgccatctca aaaaaaaaaa aaaagggcgg cc 1292

<210> 80
<211> 1283
<212> DNA
<213> Homo sapiens

<220>

<221> SITE
<222> (341)
<223> n equals a,t,g, or c

<400> 80
gaattcaaag tttaccaaat gtgcaaaatg agcagtttta ccttaggatt attattttta 60
tttatattta ctactgcaga aaattatttg attcttttttc agagaaaata ctgtttggtt 120
atattttggg gggagttttg aatttcacat acgaaagaaa taacacagcc ctttcaaact 180
gcctgtgttt caacctgcaa agttttttttt gtgctaaaga tttgagcttt gtgaaggatt 240
ccctttttgt tccttcttct ccagcaatct cagctacctg ggcgctcctg ctaatgattt 300
ctggggttcc gtgccagggg tcggcaggac aagtgtttca nttgaagctt catttggttt 360
ggagtctctt cctcytctga gccwacaaag ctcgggtcca cgggtactct gscaaaattc 420
atcatcttag ttaggcattt ggcagaatag gtgaggcagg gatgaatctt taacaaatgt 480
taatgttgct ttgctgggaa tgtgcagagg ggcatccaag atgagcacac atttaaaagt 540
aaacacatga ataagtggca gtagaattta ttttgcaact ctgagtgcta cagtgtctac 600
tgaattcagt gtattccacg ttcttattac aactaaagac tgggtagaac ggacttctct 660
taactatgca aagggaaaat ccaagacaag attccgcagg ctgctggtga aaaggggtgt 720
tatcatgcag atgtcatcct aacagattag cagagggaag tggaaatgtt cgaggatgtt 780
caatgccmcg ttgttggttw trgcaaamcc actggaaaca mcacaggagt ctaaaaatag 840
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tcgagagtca gactctacaa gggcataata cgccattttg gtaaagaaaa tgtgtatgta 1020
gatatgtaaa tagatttgga tacgaattat tgtatatacg aaggaagagt gccaaagcct 1080
acataccacg cttttaatag tttttaatct tcgttattaa agaaagattg agggagatgg 1140
gatttctgtt tttattttat acaaatctgc attgtttgaa ttttttttt ttttacgaca 1200
agctgttatt tctctgggga gtttaaaaaa aatacaaaaa aaagggaatt cgatatcaag 1260
cttatcgata ccgtcgacct cga 1283

<210> 81
<211> 708
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (40)
<223> n equals a,t,g, or c

<400> 81
aggccaggcc tccacagacc cccatggccc ccagggacgn aggggaggac agagcccttc 60
agaacagagg cctcatctca ctgcatcccc catcaccccc tagttcccca atggtcctaa 120
tttgtgttct gagatcccag tttactccgt ggccaggccc cacctgtgtt tccaagtcgg 180
gctggagacg caggatgggg taggccttgt gctctgagca accccagctc tgcctcacag 240
gcaggcaggc ccggtgcaag agtggactct gggttcctaa agcaataaat gcaaacaagc 300
caacagctct gctgcctagc aatttccatc ttagccacac ttctcccttc aggggcttcg 360
gaggagaggt cagggctaag gccggggatg agactgcagg agagagagca gcggagggcc 420
acattcggag cctccgtcca ctccagtttt atcagctttt gccttttgca cggagtgcta 480
aacaaattct agctctgtgt ttttttccca ttcccagatt tactatcagt tctccttaaa 540
aagtatctaa gctgttacag tagctttccc ttcacttgat tctattgtgt gttttctatg 600
tttggaataa ttacacccaa atatctagat attttctctt caccgcattt tgtaaataaa 660
gagatgtgta tgccaaaaaa aaaaaaaaaa aaaaaaaagg gcggccgc 708

<210> 82
<211> 1464
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (15)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (63)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (132)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (887)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (889)
<223> n equals a,t,g, or c

<400> 82
gactgtgctt gcagnaagag taaacactct cggatgccgc tgtcctgggg gagcccgcgg 60
gangctgtga atgttgatac gagctggcca gtcctgggcc cagctcactt gtccagctac 120
ctgccaggtg gntttcactg tgtttaaaat acattgcatt ccaagctggt cccctctgtg 180
tatcactcta ctgagaaatc ctgcctagtg tgttttggga tgtgtcctag catttacaag 240
aaaatgaaaa gcgtcctctt aattggcacc cgaatgttgc tgtggctcag tcacatatcc 300
aagggccctc gtcccgaggc cgtgctgccc cgagccccga gccccctctgc agctcaccct 360
tggcttgttt tccgcaaacc cggtaaacgc aagcccttgg ggcagatgca gaagcagaag 420
agggagggga aacctgcctc tgggtcaccc tgttagcaca gcgttctcat cgggagacag 480
catggaactc tctctcgcag tgctcgaggc tgtgtgtcag tgtttgctgg gcttgtggct 540
ccttttttgg ctggataaag aagtcgctgt ttttgtactg cttctgtggc tcttcacaga 600
cctcacggat gtgaccggag atgagtgccg atgaccacgt tttaaaggag aaagagagct 660
cctggtgggg ccctcggggt ggtctcaggt cacatttgca gtctgcaaca gtgacgcgca 720
cccggtccag agcgtggtga gctttgtttg ccttctgggt cggctttcgc tgtgtctcct 780
gtgtgtgtta gaatccagag cccagaggaa gtgcaagcgg gtcctccgcc aacggggaga 840
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tgaaacacct tcctgagtag tccggccttg tcaatgagtg cttgttttcc tttaaacagt 960
ctgacatatt tactcgtcac tttcaaacca gaagcatgaa aggaaggaga tattgtgggg 1020
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cctcctcctc atgaccgggg tgaattagaa cgtttttaaa gacaccccct tccaaattct 1200
gtaacacatt gtaattggag aagaaggaaa ctctgcaagg ctaaactgtc attcacaact 1260
tggctacaca tagactctag tcagttttgt ctccagaacc ttaggctttt gtatttttta 1320
attttaattt cactgttaat ccttattgtc ttttttatta agatgttgga aaagcaggag 1380
gtagttgtgc ctcaattatt gcaaaaatgt aacaataaag ttcctcaaaa taaaaaaaaa 1440
aaaaaaaaaa aaaaaaaaaa aaat 1464

<210> 83
<211> 616
<212> DNA
<213> Homo sapiens

<400> 83
tcgacccacg cgtccggtca aaatagtgga aaattagtag aaataacata ttttatatcc 60
aatttagtct ccaaaatccc aacatgcact cttctgtata cgtttttcag tatgcttgac 120
tggaacggcc aattctacag tagtcttgga agcaacatac tgcagattaa ataccttagt 180
agcctatgtt cttgaatgcg gacataaagg agcaatgctt ttcctatctt aaaaaaacag 240
tttatatgaa tgaaaacttct gttctgttta agatattata tgttgttgag tgtagttgtc 300
aaagcaacta gcacgattcc aagtaatata gaaatcacca gcttgagttg ggtctgccat 360
aacagcacct aaaacgtatc cactaaatta gtattaaatg gacaagtaaa ccaaacttcag 420
agggttgaaa tgaagacttg taatacccag tgaaaaaaaa ttattgaaac taccatctaa 480
aattaattgg aagcttaata ttacctctag gaaagagtgt gggaaatgag gaaagggcaa 540
aaggtaatgt gttccagttt gttctgttcc ataatcccag gaaatagata aacaccaggc 600
aaaaaaaaaa aaaaaa 616

<210> 84
<211> 928
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (916)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (917)
<223> n equals a,t,g, or c

<400> 84
aaaacaaaag gagacgaagg acgcatgcgt ttggtgagtc ccggattctg gtgggttctt 60
ccgctcaggc tgggtgaagc gcttccgggt cgccgccggc agcagcctcc cggcgcgatg 120
aagacactga ggctcagaga ggttaagtga ctcagccaag gtcaaacagc tagtaagtgg 180
tggagccagg actcaaagcc agtctaggag ccatgtccac tttgttcccc tcactcttcc 240
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tgcagcagca ggaacagcag catcaggcct ggctccaaag catcgcggag aaagacaaca 360
acctggttcc tattggcaag ccagcctcag agcactatga tgacgaggaa gaagaggatg 420
atgaagatga tgaggatagt gaagaggact cagaggatga tgaggatatg caggacatgg 480
acgagatgaa tgactacaat gagtcaccgg atgatggaga ggtcaatgag gtggacatgg 540
aaggcaacga acaggatcag gaccagtgga tgatctaggt agacaaggca gggtggcctc 600
agggagattc caggccagcc caaactaccc tgcatcccaa cccccaaccc ctgcccacag 660
aaccagctga tggccccagt gcctgaaagt gcccttgggc acctccttcag ctgctgccag 720
gatctggtct ctttggcccc tcccaggcca tcagtctgca cttgaaatcc ccagggcctg 780
aaacctactc caccttcctg gccagtacct caccccttga ttgccaggtc tggtctaagt 840
ttctttaata aagacaaagg agtgattttc caaaaaaaaa aaaaaaaaaa aaaaaaactc 900
ggggggggcc cggaannaat ttccccca 928

<210> 85
<211> 723
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (722)
<223> n equals a,t,g, or c

<400> 85
tattgtagtt agaaccatct gacacatagc ttttattcca ttggtttttt gttatgtctt 60
tctttacaag aatttgaagt ccatcaggcc gggagttttg tttgttgtgt ttgctgctat 120
ctcccagtgc ctaaaattgc ctggcataca gtaggcattt aataatcttt gaatcagtga 180
aaaccagatg gtggcttggc atttccacat aggaatgagc caggtggaaa tcatccagga 240
tataagtaga tcttgaagtg ataaggaagg gtcatcataa tcatgtgggg cccattttgc 300
ccttttcttgt ttcttttctc taggctcagc aacagcctca ccaaggactc catgaatatc 360
aaagcccata tccacatgtt gctagaggtg agagcagctc accccactac cagactctgt 420
gtttagggtg gtgacctgaa gaaggaagag agcgaaagaa gggaaggacc atctttccct 480
ctaaactgga gtcaagggag ggaggtcaga gcaagcctgg gggcgtaacc cagacccagt 540
ctttgttcaa tctcttctgt cctctttttc aggggcttag agaactacaa ggcctgcaga 600
atttcccaga gaagcctcac cattgacttc ttccccccat cctcagacat taaagagcct 660
gaatgccttt gaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 720
ang 723

<210> 86
<211> 570
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (6)
<223> n equals a,t,g, or c

<400> 86
gaattncgca cgagctcgtg ccgtttcatt ctgtttagaa gttcatgttc atcttagcca 60
tttggaactt cttcattctc tatcttttct ccacggtggc tgggcttgtc tgcaaatcat 120
tgtgtcaaaa tcaaactatt ttcaaaacag ccctttgctt ctgagcccct cccctaagtc 180
ctctgtgggg gtccatgatt ctgcagaggt atgggacaga atcttcagat tttacccctt 240
gagtctcttc ctagtcatat cctggttccc tcattctaat attgacaaag gatgactcat 300
taagtgcaac tggttatgta actttcaaat actttcattg tgtatgtcag gatctgagga 360
acaaaatgat gtcatttaat cggaatctaa atgtgacaca aacaacgtgc cagcaatacc 420
tgcttgtgaa ataatgttct gagcccacag tgttcctggg tatgtgagtt tatatcaagt 480
gaaaaggctg cttaattgac attaaagttt tggaatgtaa agcttcaaaa aaaaaaaaaa 540
aaaaaaaaaa aaaaaaaaaa aaactcgtag 570

<210> 87
<211> 639
<212> DNA
<213> Homo sapiens

<400> 87
gaaaaaatgc tagggagaca aaatcaaatg ttaaggggct gggctctcag cacattcttg 60
gtttgcattc tccagtgggt cagaagcctg acaatccgcc tagcctctgc tttgagcgtc 120
aggggaccca gttctattcc tgcatcctta gccatcatct acacactttt tatcttttct 180
tttaaatttt taaaaattgt gaaatctata tacatataag ccatatgttc aacttaaaga 240
atagtaaaca actgtgtccc taggatccaa gttaagaaat agatcagagt cagtttctta 300
gaagcttcta tatgtgcttc tccccagtca tgtgctctcc tgtctctacc tgagggaaat 360
tacagatttc atgcttttct ttatagtttt cctttacaca catacccttа agcctctaag 420
tactatatgg ttcggttttg caaagcccag aagcctattt taatgctgta tataagaata 480
tgctagccgg gtatggtgac tcatacctgt aatcccagca ctttcagagg ctgtggcagg 540
agggttgctg aagcctagga attcaagacc agcctgggca atatagggag acccccttcac 600
tacaaaataa aaaattaaaa aaaaaaaaaa agggcggcc 639

<210> 88
<211> 708
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (14)
<223> n equals a,t,g, or c

<400> 88
tacggacacg aggncgaaaa tgagaaaggt aacaatttcg aaaaagcatg cccttctgct 60
gtgtttccag ttgtttagat gtctgctctc catgtatata tggatcacat tcgtgttaga 120
tggaagttgt ggaatccact gttctctcaa accggtctct ttcccttgta cctatcatag 180
tgtacatagc tcaacttcct gagtttgatt ctagtgttca aagataggta tttttcatat 240
aagatgtcct gtcaaagcaa gtcattgaac ttacctggta tttaactgaa aacaaacaaa 300
aatcagcaat ctcttccatt gcttgtagaa atactgactt aggccaggca cagtggctca 360
cgtctaatcc cagcactttg agaggccaag gcaggagtat catttgagcc caggagttcg 420
agaccagcct ggcaacatag tgagaccttg tctctgtaaa aaggaaggaa ggaagggaag 480
gagggagggg tggagccaga ggaggggagg ggacactctg ttatacttat cgaaaggtgc 540
tatccaggtg tggtagtgca gccgatagtc tcagctactc aggaggctga ggtgggagga 600
tcacttgagc tcaggagttt gaggctgcag tgagctatga tggtaccatg tactccagcc 660
tgggcaacag agacagacca gactcctaaa aaaaaaaaaa aaaaaaaa 708

<210> 89
<211> 949
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (55)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (508)
<223> n equals a,t,g, or c

<400> 89
catgataacc ccaactcgaa taaccttcac taaagggaca aaagctggag ctccnccgcg 60
gtgccgccgc tctagaatta gtggatcccc cgggctgcag gaattcgsca cgaggttgtg 120
tgtgtgtgtt gcttgggtgt ttgtctcctt tgtaatggtc gtgggtgaca agtgtgtcag 180
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gtgtttgtgt gcaggtatat gctttcccta tatgtttctt ttctgacttg atttgtgact 480
agctgtgtgt gtacacggct gtgtgcancc atttgctgaa atgcagttgt gtgtgtgtgt 540
gtgtgtgaga gagagagaga gaggagagag agagagaagg agactatggc ttttctgttt 600
gkmcaaarrt catgtsagcc tatgagtgcc tctctctgtg actggagctg tatgtggtta 660
catgtggtca caagtgcaca ttcaagttca catacacaga gatatcattt tagggcttga 720
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ctgaacctgg atcgtgtgtg tgggaaagac ccaggaccca cacacaatgt cakcagctgt 840
gtgtaattgt gtgctctgtg tgtggctgtg aatctgtgtg tgtgatttgc ctgttgattg 900
tctttggcat ggctgtgggt ccacgggcgg tgaggttcag gagtctcga 949

<210> 90
<211> 1171
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (291)
<223> n equals a,t,g, or c

<400> 90
gaattcggca cgagcctctc cagtgcttac gtaaagaaat gaaagtattc agggaaagct 60
gtgctttgtt ggaggaccgc gttgtggatt tggccacctt gtcacttgaa gtcgtgttag 120
gggtgcttca gcaggatgtg gccggatgcc tttcatgatg atgctgcaca gmaaactgtt 180
gctctttstg gaagctttgt ggtactacgg tgggggggct ttcctttgct gtgccggctc 240
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gcagggaaac cagaggctgg cgtyctgttt tctttktgta aaatggaaaa atacctgcca 420
ttgccactta actaagtcac tgaagagatc atgtgcatgg aagatgtaaa acagtatgcc 480
tctttataag taaggtggca ttattacttg agctggtgga aggcagcacg tttcccacaa 540
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cagagttggg ggtgcgattg tcgatagtag gctttgggag aaatgatkgt tatattycgt 660
aataaatgat gtccttgaga aactcataag ttgcaatgta atcctgtctt aattgtgttg 720
ggcacractc ccactgcaat accttaaaca actgaaaaca tttgccttty aaagccccaa 780
tcgacttgga caataaaaac agttgcatgt tttgctctag agatattttc tgccgtttcc 840
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ctgtagttag catgaaaaca aattgccagt ttgattttct aggacagctc aagcagaatt 1020
tgtaccacta ggctgtaagt tttaagtatc taatttctg atttgaaagt gtatgattta 1080
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aaattacaaa aaaaaaaaaa aaaaactcga g 1171

<210> 91
<211> 1151
<212> DNA
<213> Homo sapiens

<400> 91
ggcacgagtg tcaatgaaag tgtttctaat gcaactgcga ttgactccca gatagctaga 60
agtttgcaca tcccactcac ccaggatata gctggtgacc caagctatga aattagcaaa 120
cagagactca gtattgtcat tggcgtggtt gctggcatta tgacggtgat tctaatcatc 180
ttaattgtag tgatggcaag gtactgcagg tccaaaaata aaaatggcta tgaagccggc 240
aaaaaagatc acgaagactt ttttacaccc caacagcatg acaaatctaa aaagcctaaa 300
aaggacaaga aaaacaaaaa atctaagcag cctctctaca gcagcattgt cactgtggag 360
gcttctaagc caaatggaca gaggtatgat agtgtcaatg agaagctgtc agacagccca 420
agcatggggc gatacaggtc cgttaatggt gggcccggca gtcctgacct ggcaaggcat 480
tacaaatcta gttccccatt gcctactgtt cagcttcatc cccagtcacc aactgcagga 540
aaaaaacacc aggccgtaca agatctacca ccagccaaca catttgtggg agcaggagac 600
aacatttcaa ttggatcaga tcactgctct gagtacagct gtcaaaccaa taacaagtac 660
agcaaacaga tgcgtctaca tccatacatt actgtgtttg gctgaattcc actctaatat 720
gatgctccat tatgcaccat actgtgatga cctttctact ccgaaacctg ctggagcctg 780
cccttggccg tggggtgtca gccaatcact gcttgttcca cttgttgtac attttatttt 840
tgagtctttt tctttctcat atacagaaaa atagtatgaa aataaaataa atgtatgaaa 900
cagtattaat gcagaaatgt gctactaatg gatgtctgag tcaccagaaa ttccattctt 960
aaagaggcgg ttagcaccta ttagacgtaa cagtgatgtc ttttaaaaaa tccaaaagca 1020

tattgcaaca ataagtttga gactttgtgt gaacaaaggg aaattcagcc tcttatgtct 1080
ttgtctttaa tacattaaat actgattttg aataaaaatc taaattgatc aataaaaaaa 1140
aaaaaaaaaa a 1151

<210> 92
<211> 714
<212> DNA
<213> Homo sapiens

<400> 92
ggcacgagta atgcttctgt ttctcccact atatgcatat gtatgtgtgg gtacgtgcac 60
atttggtttt ttatttgttt gtgtgtctat ctgaaagttc tgcagggcag cgcttgccct 120
tggattgctg ctgcagtggt gatgagaagg atgaggaaag tgcaggaaaa aggggaggtg 180
ttcaggaaca tggcggccac ctgggccctt cgttctggca tacaaagcct gaattctctt 240
gttagctctg ccttttttac tattttcatg accttgggct cttcttggaa cctcattgtc 300
tcactttcct cattggtaaa ttggaccggt ctcttttctt tctacttctc aagaaactga 360
tgaggattaa tgagatagaa tctggagccc gttttgtgtt aaaaagagtt aagggatgct 420
agaagacgga gttaatgtca tagagaaggg gaacacacat tgcttaccgt gtgatgtgat 480
agagtctcag ggagcacttc tctttcaact gttaactgtt aactagttgg gcaggtggca 540
gcctcatttc tatttgtgtc tgaagtggat gacatgttag tgcaggatga taggaagtca 600
aaccaaatgc agggactggt ggaatgacga gtcaagattc atgggggaac atctagcctt 660
ctgcattgct acctgaaaga aacttagcta tttaaaaaaa aaaaaaaaaa aaaa 714

<210> 93
<211> 810
<212> DNA
<213> Homo sapiens

<400> 93
ggcacgagtc ctgcctcatt tttctgtggg cctcatttgg tatgcaagga aataagccaa 60
acagcctgaa agtccagtag aagtgacagc cagacatccc agtcctccct gtagggtttt 120
ctcagaactg ttccttttaag gtctcaggct gctggaaggg agggctgata gcagaaaaag 180
tggggacact gggaactcca aagggaagac gcgcatggcc tgaaaccgag ttctttcgct 240
ttctggagcc tggtctccct atgtggaggg tcatgctggc atggctggca atggttaatt 300
caccgatggc catggagtcc caagttggcc atattattgc ggtaaaagat acattaaccc 360
agatgacctt gccgggggcc agaatagagc ccgtgaggaa ggagagcaag gcaggatcgg 420
ccgggaagcg agagggattt tgttgaggag caaggtcttc cacaggaact gcgacttgga 480
aagtattcac caagggctgt gccatgcgaa accctcttta aaggaaccgc atcgtacgcc 540
taacgggcat ttctttttta atgtaatggt tcagagctat tgtctaccac gcctcgcgtg 600
cacacgcaca cacacgcaag ttccctcagt cagccgagaa tcctgccatc tcttttagat 660
aacaaaagct cttaggcctt atgctttggg taggatttgt cttccatgga caggtattca 720
gttggaaaca agtatatagt cactgcctct atggtatgga gatactccga tttagtccct 780
ctgcctcttg gggaaaaaaa aaaaaaaaaa 810

<210> 94
<211> 1176
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (569)
<223> n equals a,t,g, or c

<400> 94

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gtgaaagtac attacccgcc tccctgcagt tttaacccta tacagtggaa gtgtagcctt     120
tccttcttcc aggaattgtt agcataaatc ctgacagttc cagacagtat ggaaggatcc     180
cagtagatag ggaaaagatc cccactcgaa ggtccaagcc tagtgggata cctttcctgg     240
gcacatggtg ccaagagatg acttaaatat ctacaaccac ttgtcagctc agttttttg      300
gggactactc cagaggtgtt ccctcacaga ggcagtggta gaaaaagtaa ggtagaaaaa     360
agcagtaaga cagggatgtt tggacaaggc actcattcat aagaaaggaa tgatagcaga     420
ttggatgttt tttgtttatg ccttatgtat tgacgttact gccaatgaat tttgccttac     480
actgaccttt ttaacgtcaa aagtgtcaaa atagatttgt tgttgttgca gttttgtaat     540
gggcgggtgg tattattaat ccgggatgna ggctggattt atttttttatt ttaatttttt     600
ggcttggctg acctggaaga tctactagct ctctgccctc acggtccaag gtgtgttctt     660
cccccactga cagttgggct gctgatggct ccctttttaat tcccatcagc tgagggctga     720
ctcagtcaac atcttctccc catcctggac cccaagaata caggaaaaag gctcagagac     780
ttagcacatt atttttgttt taagatgtca gcacctgatg tattatttta gtgcttgttt     840
aaatattctg aaactgtgtt ttctttttttc ctttaattta aatttgtctt cataaagttg     900
gcttacaaga acatttcttt atcaagttta tctggatttt ctgggtcaaa agtataagtg     960
atttctggac ttttcttgac aaaaagtacc aagaaaagct gcattaaaac aacaaatcta    1020
attttaaaaa cacttagtga gctaaaacgc agactcaaac caaactaatg aaagctattt    1080
aagagaagtc agttgaagta gtttccagaa tttatttcat tgtttttttca actctttgtt    1140
aacaccataa acgtgaatta aaaaaaaaaa aaaaaa                              1176
```

<210> 95
<211> 1028
<212> DNA
<213> Homo sapiens

<400> 95

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gcatgatcct gtggaacaca gtttgggatc atagatgtga attaagacac caccgagata      60
cgggctgtga ggttcatacc gtgctgatag cactcgtggt gtctgtgaaa tgtgggtaag     120
acattcaaac ctggttttga tactggaaac tcttccttta aaactgtgac catgatttca     180
ttcagcccct ccacacccct atgtctgcct tgtttcagag tgagttttct atggagcctg     240
tggccctttt gcagcccacc tggtggcttc ttaatgtaac tcttcccctg gtcgcctgga     300
gtggaccact catctgcagg cctctcctgc atggggaggg taggcaggga gcagcatgtc     360
tgcaggggtg aacctttgct cttctgtcag gcgaggccca ggctgcacca gccacctgcc     420
acatggtgac agtgccacgg gccctgcgta tggcccctgc aaccgtgctc tggcgggcac     480
acctggctgc tgcaggccaa ggccgctgtt cagtgaagag tcccatgttt agtatggact     540
aaagtcccat gtttagccay tgccccagtc tcccgtgacc ccagaaacca ggtcactgga     600
ccacagtgcc agatcctcat cacgccggcg agcacctaga agtgagaaca ctgtattcct     660
acaatgtaca cttggatatt tctccttatt tagtttctag tgaaacaaat caagtaagga     720
actatcttta gtttagatgg aattatttgt ttttaattgt tgccgtattc atctatatag     780
ctaatatttc aagataagta atgaacaaaa cctgtctaaa ccttttgttt ccaatgaatg     840
aaagtcatgc actttattta taggctctat gttttggctt ctgcagtact tttattatct     900
atacataatt tggccaaaaa taagaaattg gaaagaatga aatgtttagt ttatagtaga     960
agaaagatga tgacactaag ttgtgaaaat atgttgtgat ttttatgaaa taaactcacg    1020
gcacgtag                                                            1028
```

<210> 96
<211> 747
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (605)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (642)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (645)
<223> n equals a,t,g, or c

<400> 96

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tcgacccacg cgtccgccca aaggaatcct gagtatgtat gcactttaaa agaacccaga       60
atcatctaaa tattgtcaca tggctcttgc aagtgatgat aatagtgatg cttataataa      120
tgaggattag ctgcactcat cagcctgtag aaagtaaaaa gtttcctttt cgaaatttcc      180
tttcttgtta agaataaatc ataagtgtta gaaataatag tttcttttaa agactaactt      240
ccttcaagcc ttctctgctc tgtgctaata actcttcgtt aagccctatc ctatgtagct      300
gttagatata agggaataag tatattctat gtcctgtact ttagccaaga tatttgtgct      360
ggacatgctc acaggcacgt tccagctggc agcctatgcc ccttccttat ttggaaatat      420
tattactttt ctaagtcttt ttgcaagcaa cttcttcttt tcctttgttc tctgttgcct      480
ttccctatat aggaaagttt taagttatta gccagtcggg tttaatttaa attgtgaggt      540
ccagctccag ccaatggaga caggacacaa gctgcataag ggataaaaac tgcttccctc      600
ctttnttcgg gtgtgctgtc accattgttt catctgtgag gngcncccctt tctgccagaa      660
agtaaaattg ccttgctgaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa      720
aaaaaaaaaa aaaaaaaaaa aaaaaaa                                         747
```

<210> 97
<211> 628
<212> DNA
<213> Homo sapiens

<400> 97

```
cggcacgagt atatatatat tttttaatat atatataaaa agacttttag atagaatttct       60
catattctga tgacctatca cgttgtttgt gcatttttaa tcgtggtgct aaagaaacag      120
tttatactag ctctgcagac tatttcaaca tcactcagga gcaaacaaat tcttatggtt      180
ttaagcagta ctattattgc agattcaacc ttttattatt aatacttaaa aacagggaaa      240
aggttataag atgtggagct cattggagag taaaattaaa ccaacaaaaa ggatatgaca      300
aagtacaarg gaaaacaaaa ccaaaaaact tcatgtatcc caaaaaatta attttgccga      360
taaatgcttt aaaagtgggc aaaaaaggag gtttctcagt agaattattc gcaactaaag      420
gcaaatggaa aactctcaca tagcatttaa taaggtttta catgcaatat atcccactat      480
cccaagaaat atctgcagtt caaagctgct ttttaaatta atgcttccta gtgtttgctg      540
tttataaatc ctaaatatta aagggtgagt tccttaataa tactattcta ataagtacta      600
agacttttct aaaaaaaaaa aaaaaaaa                                         628
```

<210> 98
<211> 904
<212> DNA
<213> Homo sapiens

<400> 98

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ggcacgagat cgtcttgtga caagacttgc tgagaagcac cttaaaattc actgtgagcc       60
acattttgtc ttttactgtc tcatcggata gggtagatca atgtcctta ctgtagcaga       120
gactctctca tgggcaggac catcatggaa agttctgact acatcaagaa aggcgccaat      180
gtctcacctg tgcttggggt caggcagcag gctgtgatgc cggtgcctct ctggttggta      240
ctgtggttct gcttcctgtt atatgtagcc tcacgaagga cctttggatt agccaattac      300
atgcccctac cctgagcttc ttccccagct ctttgacttc ctggacattg gtgaatatcc      360
tgaataagca aaagggataa aattcataga aatatggtgg caaaaatata caacttcagc      420
```

```
ccagttcttt gggtccatgt tggtaaggag tccagttggc aagacaagct gcccaaggaa      480
gtgcctcaga agtctgggtc aaagaggagg gccagatctg ttctgtgaga ccctatgtga      540
ttgttatatt tttaaataat atataattaa gcaggacaaa ttaaatactc catggctttg      600
gggaaattgt tgctttaaag tcctggaatg gggctgggca cggtggctca tgcctattaa      660
tcccagcact ttgggaagcc aaagtgggtg gatcacctga ggtcaggagt tcaagaccag      720
cctggccaac atggcaaaac cctgtccatg gtggtgtgcg aggctgaggc aagaaaatcg      780
cttgaacccg agaggcagag gttgcagtga cctgagattg cgccactgca ctccaacctg      840
ggtgacagaa tgagactccg tctcaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa      900
aaaa                                                                   904
```

<210> 99
<211> 576
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (12)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (521)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (535)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (572)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (576)
<223> n equals a,t,g, or c

<400> 99

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aaattccccg gntcgaccca cgcgtccggg caacattccg ttacatagag aaatctatgt       60
aataagctgt gtcataacac ccatcagttg tatttatgat ctttattaat gtattttgtt      120
tttaagatct ttttcagag cctctgtgtg ctgggttact gtatacttcc cttgacagta       180
gcaatgctga tttgccggct ggtacttttg gctgatccag gacctgtaaa cttcatggtt      240
cggctttttg tggtgattgt gatgtttgcc tggtctatag ttggtaagta tgtacttatt      300
tccacaataa cagaacagac aaaaacatga tttaatgatg aagaccagat gaggagcagt      360
ataagtccaa agttagatgt gagtgatatg attcttgata gtattatcca tagaaccctc      420
ttccctgagt aggcaatgat ggggcttatc tgagttggat atctggactt ataagatgtg      480
gagagtcaca tcktttttct ttctttaaaa aaaaaaaaaa nggcggccgc tctanaggat      540
ccctcgaggg cccaagctta cgcgtggcat gngacn                                576
```

<210> 100
<211> 713
<212> DNA
<213> Homo sapiens

<400> 100

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ggaagaggtg caagcaaagg ttttacgtat gatcaatgtt tactttagcg gccctggggt       60
gctaacgcct ttggatgacc aaggctcacc ctgccctccg gcacctttttg ctgctcttca      120
cccttgccct caccctgctg gctcaggggt gctgtgctgt tgccccctca ggctgtgccg      180
accttgcagg attttgttca ctgggccact cctgctgacc cttcaccatc tgctctgtga      240
aacctctccg agtggtatag gagttggaaa catagtccct ggggccagac ctttgggtgt      300
aaatccagtc tttcctattt ctagctgtga ccttgggcaa gttgctgagc cacttttggt      360
gaccatttcc tcctgaaaat gaaactaatg atagtgccta cttcacaggt aaataggagt      420
atgaaatgaa ttcacatata taaagcttct agagcatctc ttctcagtac ccaacatcct      480
gattactaat ttgcgggggg tggcactctc tcctcttttt ctctgctctt tgcaggtgct      540
gccaccacta acaataaact atagggagga gaaacccagt caattccctg aaaagtctcc      600
agtgtgacca gaagtacaga taatattgtt ccattgtatt aaagtcattc tagggagtct      660
tagaagatta gatgcatgtt ggttcctaca gaggaaaaaa aaaaaaaaaa aaa              713
```

<210> 101
<211> 649
<212> DNA
<213> Homo sapiens

<400> 101

```
ggcacaggga agtgtcaagc gggcgctccc ccatctccgc cgctattacc actgaacccg       60
gaccccctac ccaggtccag ggccagccgc catgacgaac gtgtactcct tggatgggat      120
tctggtgttt ggtttgctct ttgtttgcac ctgtgcctac ttcaagaaag tacctcgtct      180
caaaacctgg ctgctatcag agaagaaggg tgtttggggt gtgttttaca aagccgctgt      240
gattggaacc aggctgcatg ctgctgtggc aattgcttgt gttgtaatgg ccttttacgt      300
cctgtttata aaatgaattc caaagcaccc aagtcatcaa ctgccaacca aggggacggg      360
gatgaagaac ctgttggaga cctgaaccca gtgtaggaga gttcagctga aatcatcggt      420
ccccaggatg acaccacagc atctgcccct gctatatgtg gggaaaactc atggtcacga      480
acattattta tgcttcaggg gactacagaa agccagcttc ctttgatcta tgtgtaaatc      540
agtccttggc agagtgcata taatgtccgg ataaattaca cccctcggtg ataagattac      600
atacctcctt cataaaaacc tgtaaaaaaa aaaaaaaaaa aaaaaaaaa                  649
```

<210> 102
<211> 697
<212> DNA
<213> Homo sapiens

<400> 102

```
gatttaggga gggggctgtg atgtaaaacg tctcccctgc caaaggaggg gcaaagtgct       60
gtgtcagttc ctgtttcttc ccatttcctg gcacactctg ccccctctgtc cgggggacac      120
gcgcatgtgt ttgccaggga tggggccacc gggttgatgc caacgctccg ggtgcctgtc      180
ttgtctgtgt ggcttctcag atggtggagg gtgctgggag ctggcagggt ccttccagac      240
agtctcagcc tctccccgcc gcccccaaca ggctgtcaaa caaaaccgga gagggggtgg      300
gggagccagc ctcccagcgt gctgtkcccg caggcacccg tgtgacatcc gcacgtccag      360
ctccgtgacc tgtgtgtgtg tgtgtgtgca caagtgagtg agagatttcg aacgcccacc      420
cctcgacttt gaaatctgag caaaacaaga aactggggtc ttcctctccc ccgaacctct      480
ccccagctag tcttccctct gttcttcctg cctccagccg cccgcgccag attttgaaat      540
ctcggagaca aaactagtac tgtaagataa attttttgt actgtattta ttgtgtataa      600
cgatttttt aaaggagaat tctgtacatt tagaactctt gtaaattaaa aaccgatcct      660
ttttttaaaa ctgtaaaaaa aaaaaaaaaa actcgag                               697
```

<210> 103
<211> 1288
<212> DNA

<213> Homo sapiens

<220>
<221> SITE
<222> (462)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (813)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (825)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (834)
<223> n equals a,t,g, or c

<400> 103
cgatgaaggg gtacagggag aaagattatt taggatcctg aggatcaatg gagaaaaacc 60
atacaacttt gttgattact ttcactgtga atacatggtc tactacctca accgggccct 120
cagagctact ttcagcattc tgttttccgt agtttgcttg ctcttcctgg gttccatagt 180
gaactgtttt ttaaatgatg tcttcaagcc actgaccctt aacttttcca ccgcactctc 240
agcatggaga aaagagtcat cagcctggaa ttcccttggt ctcctaccac caacagatga 300
atatcccaca tgagcatcca ccttcggccc ctttcctagc tcagtgggct tccttcctat 360
tagtgtctgg ttttctattc cattcagttc ctacccttcc tgcctgctca gagtcctcac 420
accttatgta actgattatc ccctttwctg tttttggctt tngtttttt gagacaagtt 480
ctcaccctgt ccccaggtta gagtgtggtg gcataatcat tgctcactgc agccttgaac 540
tcctgggctc aagcgatcct cctacctcag tctcctgagt agctggaact acaggggtat 600
gccaccttgc ccagcttatt tttcattttt tacagctctt cttttaggtt cagggataca 660
tgtgcaggtt tgttacatca gtaaatgcat gctgcaggag cttgatgtac agattatttt 720
gtcaccaagg taataaacat agtacctgat aggtagtttt tgaatacccc ccctyctccc 780
accctccacc ttcaagtagg cctcactgtc tgntrgtccc cttcnttgtg tccntatgta 840
ctcaaagttt agctcccact tataagtgag agtatgtggt atttggtttt ctgttcctgt 900
gttagtttgc ttaagatatg gcctccagat ccaaccatgt tgctgcaagg acatgatctc 960
tgtctttta tggctacata ggattccatt gtctatacgt accacctttt aaaatccagt 1020
ctatcattga tgggcattta ggttaattcc atgtctttgc tatagtgaat agtgctgcag 1080
tgaacatact catgcacgtg tctttatgtc agaaacatat ttaaactaaa gagcttctgc 1140
acagcaaaat aagctataac agagtaaaca gacaacctac agaatgggaa aaaatatttg 1200
caaactatgt atccaacaaa gatctaatat ccagacgcta taaggaactt aaacaaattt 1260
acaagcaaaa aaaaaaaaaa gggcggcc 1288

<210> 104
<211> 1027
<212> DNA
<213> Homo sapiens

<400> 104
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tttaactttt ttaaatagat ttatgtatgg tagtaaatga tagactagta tctacatgta 120
ttttatgtac tcttcacata cctttatttt ttttgatatt tctagtctat gaggttcatc 180
tggtttttca aattgttgca aatctccaaa aaattttcca atacatttat tgaaaaaaaa 240
tccatgtata agtggaccca cacagttcaa acccaagttg ttcaaggatt gactatttgt 300

ctatctaaac atacctaaac atagraaagg tacagtaaaa atacagtatt ataatcttat 360
gggatcacca ttgtctatgc aggctgacat tgaaatgtca ttatgtacag catgactgta 420
tagtgtttcc gagttctgtg aggctctcta gcaaactaat ggagctcaag aaggggttat 480
gggaacccta acttatagct agttggttag gacccttggt caccatctgg ggcttctgat 540
tgtcatctga agtgggagcc atcttgtggc actgagcytt caacctatgg tatctgatgc 600
tatctccggt agtgtaagaa gtgaattgaa ttagaggaca cccagctggt gtctgctgca 660
aaattgctta tttgcttaat gcgtggggaa ccccccctcca cacacatctg gagtcagaaa 720
gggtgttgtg agattaaagt gggagaaact gaatttgttt attcctatat tcagaatggg 780
gtccttgara acatcatagt ggtaagcata gatgttctaa agtcagactg cctgggttca 840
tctctctgct ccaccacttc gagagttact ttagctcact gtgcttcagt ttcctattaa 900
attgggataa taataccatc tcatagagta acttaagaat taaatcagtt aatatacata 960
aagcacttgg aagtgtttga agcattaata aacactcaat agctaaaaaa aaaaaaaaag 1020
ggcggcc 1027

<210> 105
<211> 710
<212> DNA
<213> Homo sapiens

<400> 105
ggcacgagct gggcctccag gttcttcacc tgtcacatga tcattttaca tattgtggtc 60
tgtttattta ccatcagcat catagaagag caaaaagaag aaatactgtg ctccactaaa 120
agccaggctg agaaaacagt tactcacatt gagcagtgag tgaccactag gtgggcattt 180
gttcatagct gcatggagaa caagtgccca tatacatctt tctgctgatg cagcctctaa 240
attttgaatg catcagtttt ttaaactgca ttgagcaata ttccgtgggt gtgatccata 300
atagcgtaac tatttacgcc tgtgacagag aggaaaactg tatggatatc agatatcttt 360
aagagctttt taatctttaa tcaagttagt acttcttaag gatgattaag gccaggcagt 420
ggctcacacc tgtaatccca gcattttggg aggccaagat gggtggatcc cttaaggtca 480
agagttcaag gccatcctgg ccaacatggt gaaaccccat ctctactaaa aatacaaaaa 540
ttagctgggg tgtggtggca ggcgcctgta accccagcta ctcaagaggc tgagacaaga 600
gaatcgcttg aagccaggag ttggagattg cagtgagcca agatcatgcc acttcactcc 660
agcctggaca gcagagtggg acttcttctt aaaaaaaaaa aaaaaaaaaa 710

<210> 106
<211> 530
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (16)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (22)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (45)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (47)

<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (54)
<223> n equals a,t,g, or c

<400> 106
ttggccccc tagggncttt tngccaaaaa aggctatttt agggngnccc cctntaggaa 60
gggtaccccc cttcaggtac cggtcccgga attcccgggg tcgaccccac gsgtccgccc 120
cacgsgtccg cttttgtttg gagaacagct ggctaaggat gactctaagt gtactgtttg 180
catttccaat ttggttaaag tatttgaatt taaatatttt ctttttagct ttgaaaatat 240
tttgggtgat actttcattt tgcacatcat gcacatcatg gtattcaggg gctagagtga 300
tttgggtgat actttcattt tgcacatcat gcacatcatg gtattcaggg gctagagtga 360
ttttttttcca gattatctaa agttggatgc ccacactatg aaagaaatat ttgttttatt 420
tgccttatag atatgctcaa ggttactggg cttgctacta tttgtaactc cttgaccatg 480
gaattatact tgtttatctt gttgctgcaa tgagaaataa atgaatgtat gtattttggt 530
gcagacacct gaaaaaaaaa aaaaaaaaaa aaaaaaaaaa gggcggccgc

<210> 107
<211> 392
<212> DNA
<213> Homo sapiens

<400> 107
tcgacccacg cgtccgccca cgcgtccgga gggaacttaa atgatattcc ccttttcctt 60
ttccctaata accttcctgc cagattttca agtaggcaat gataacagca ggtgagatat 120
taggaactgt gactacgaat atgtagatgg agatgtgcag aaggatccag agacttagag 180
caatgcttca catgcttttg gtaagcatgc tccctactgt gggtaaacca aacatgtacc 240
aacccccca gaattatgat attctactgc agtaaccagc ctcttctttt aacatcagat 300
agctaaagga cgttatcctc aaagtcatgg aaaagcagga agtttttcat gacaaatcag 360
tttgccatag tacagttaaa aaaaaaaaaa aa 392

<210> 108
<211> 991
<212> DNA
<213> Homo sapiens

<400> 108
ggcacgagga attttgtcac gtgagctgtt gggttactga gtgagtgaag ttcactgtct 60
gcaattgagc ccttttgagg attcttaaaa cttcagcctt tttcagtctt tccatctcat 120
tccccttaaa gaaacacatt tggactttgt ctggctctct ggtaaaccct gtgacctgca 180
ttactagggc acagtgacac agaaaagaaa gtgtgtgttt ggtaaatatt tattgagcac 240
ctgcagtctt atgtttagca gtatgcatgg tgcctgctct tggaaagcaa agcaaaccag 300
ttcatcagca ggttttcttt gcctgcatgt sctgtgccca gccttgcagt tgacacgaga 360
gaaatataaa acatggccct ggccttcctt catttaaaca tttctytttc ccaagcactt 420
actctgtgca aggagctgga gaagccaaag ctggagaaaa acaaaggagg gcctgccctc 480
gagaagttag tggtctaatg ttgtggttct caaactcagg cgtgcgtttg aatcgtctgg 540
gggccttgcc agaccacaga acccatcccc tgagtttctg aatcaatggg tctgaggttg 600
ggctcgctga gaatttgcat ctttataaat tccagataat ggtcttgcgg ctgggtaggc 660
accatggttt aagaaccact ggtctggccg ggcgcggtgg ctcacgcctg taatcccagc 720
acttcgggag gccgagacgg gcggatcacg aggtcaggag atcgagacca tcctggctaa 780
cacggtgaaa ccccgtctct actaaaaata caaaaattag ccgggcgtgg tggcgcgcgc 840
ctgtagtccc agctacacgg gaggctgagg caggagaatg gcatgaaccc gggaggcgga 900
gcttgcagtg agtcgagatc gcgccactgc actccagcct gggcgacaga gcgaaatccg 960
tctcaaaaaa aaaaaaaaaa aaaactcgta g 991

<210> 109
<211> 912
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (896)
<223> n equals a,t,g, or c

<400> 109
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ccccacctcc cttagccccc cctcctctgg cagcctctcc tgcctctgct gagctccccc 120
ccacgtgttc caccccctta ccctgctgtt gtttacatcc aacctgcctg agaatttcct 180
ctggggagga atctattcct gtcatggtct agtgcctggg agggagagaa ctttctgggg 240
gtagggtgcc ctccatctga aacaggccag gtgagcatca tgcayaaggc ctccattctg 300
tccgctcaga ttctgggtgg ggccacaggc aaatctcctg acttatgggg agttggcttg 360
tggttcctcc cttggatagc ctccatggaa ccactatagg ctttcccaac agctgcctct 420
gaaatagctg ctgcttcgag atcctccctt tttaaagcac tttctaaagc cctcaggatg 480
gcgggagcra acagcactgg tatattctag gagtaagtgc aggaattcag cagtgagagc 540
atgtctggga ccacctggac tgccatccat ttaacctcaa atctctttgg gatactcgcc 600
ctccctggga accagagttc tggctctaac attgagcagc tatgcactag ttccagagaa 660
gccactaaca ggctgccatg tgtagatgta ggttcttaag agatcacagg ctgggtcatc 720
tgatcactgg atggatagct cagcctgggg catttagtgt tttccctggt gataaatccc 780
caagrcagct ggatttggag ctggtggcaa gttgaaatta ttaaaaattg atttgtgtgg 840
gactgtcaaa aaaaaaaaaa aaaaaaaaaa aaaaaactcg agggggggcc cggtanccaa 900
ttcgccctat ag 912

<210> 110
<211> 875
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (66)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (872)
<223> n equals a,t,g, or c

<400> 110
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gctggncgtg gaaatgggag gcggttgcag rgggtctatg gggcccggtc ctggatactc 120
ggcaggaagc cgtgtctgca gaggctcctc cctgcctcag gtggccccgt tcaaccccag 180
ccgtgcccat ctcctgccac cgcctgtcgg tgggggttta aattcggtgt ggctttctgg 240
ggtgcagctc agcacccccc cttatgcaga ctgggagggg gtcgggcagt cccctcagcc 300
acgaggaccc tggatgggtt ctagttcact tgggaccgtg gggcctggct gcgtactgag 360
tgggtgcccc acagtcaagg ccaacggggg ctccccctgc tctgagatgt tgggagaaag 420
gcggcttctg gaaccttccg tgggacccgt aagtggctgt ccagaaaggc gggagggtgg 480
gcacggggca cgggggggcag ctggggtcgt cgttaagggt cacgcatccg tacagttgaa 540
tttcctttct cttatcatgt tttacccacc ttgtcccttt tttccccaat tgtgcttttg 600
catttttttc cttggcaaat gtaaactcag cctttcattc atgacgtgtg aaatttcagt 660
ttctctggag tttgtcagac ggcgtgggaa ccacgcctga aactcaggta ataggaggaa 720

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aaaaaaaaaa cttaaaaaaa ttttaaaaa acataaaact actctctacc tctgctggsc      780
cagcctgtct cgccctggcc gcggcagggt ggcctgtaac aatttcagtt ttcgcagaac      840
attcaggtat taaaaggaaa aaaaaaaaaa anggg                                 875


<210> 111
<211> 459
<212> DNA
<213> Homo sapiens

<400> 111
gggtgagaga gggaggtacc agagtaaata cagtgccact tggatggtga caccccatta       60
ccttcagaca caaagatgta agctgaggga aatgaattct tggattcagg gaaatgaatt      120
cttggattct gaacatgagg gtcagattta cattcctgtc tcaattgttg acgcttatcc      180
caaggactag tcattctgca acatctgtgg gaaattccca gattgaactt cccagggaga      240
aacatcatat gacatattgg gaaaatggct gacaatggtt ttccttagta agttcattga      300
gaagaaaagt gggcggatga ttttcccagt cttcactctt tcagaagccc ctaaaacaat      360
ctgacatgct ctagttggag cctgctttct atcccatcag tttgatttct gaatgcctta      420
tgatcattag cattcttcat taaaaaaaaa aaaaaaaaa                              459


<210> 112
<211> 609
<212> DNA
<213> Homo sapiens

<400> 112
ttctgttcat ttttccccct ttctccccca cattcattaa gaaccctact gaaaccctag       60
gtgacaaaag gtgtgccttc tgttgccaca tttgacccac cacaggactc actggactgg      120
acttctattt atatggtatt aagtaactga tatatatata tatatatakt tttgattgac      180
accaaaaaat taccttggca caaatgccag acctgtgaag gtcagaggcc cgctgcttyt      240
cccaggaggg agggaacttt ttggttgtct gtggcaattc ctctgtacag attgtaactt      300
tttaaaaatt tcccttcacc ccgtcacttg aatatatgtt catagtaatt tgtaagatac      360
ttctttttct tattttggtt gcaagaccct tccgaacaca ttcctgtata aagtattttg      420
cactatttaa agaaacccat atggatgaag tcaggatgtg caatatgatg gcgtcacagt      480
gctcatcgtt gtacctgtaa tgtaactaat cagtttaaat gtactatttt aaatatgtaa      540
aataaatttt caccatgagc atgttttaat gaaaaaaaaa aaaaaaaaaa aaaaactcsa      600
gggggggcc                                                              609


<210> 113
<211> 1404
<212> DNA
<213> Homo sapiens

<400> 113
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taagagtccc atcttggcct tctaagggaa agataggtaa atgaaaagac tgctaaatcc      120
aaggtcagac agcatataga aggctttata aaagaacagg aaaactcaga acactaaata      180
agagagtgct ttcttggact ctgcagttgg cctcaatcat cggatctgga atattacttt      240
ttacgatttt gsaagccgat acacacctgt aagtaataac tgaggaaggt agagtatgat      300
tagtcttttt acctttcagt gtgtatcaat gttaagtgaa caagagcmaa aggaaaacca      360
tatatttagt attttgcaac atatataaaa taacaacact gggctgggcg tggtggytca      420
agcctgtawt cccagcaytt kgggagccga ggcaggggga tcacaagktc aggagtttga      480
gaccagcctg sccaacatag tgaaaccccg tttccactca aaatacmaaa aattagtcgg      540
gcgtggtgat gggcacctgt aatcccagct actcgggagg ctgaggcatg atgatcgctt      600
gaacctggga ggcagaggtt gtcgtgagcc gagattttgc cactgcacac cagcccggga      660
aacagtgcga gactccgtct taacatgaaa aacatgaaca gccgctacta tctgagggca      720
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atttttgtc tttatacttt ggcatgtata ttatttctac aaataatttt aaaggccagg      780
tgcggtggct cacgcctgta atctcagcac tttgggaggc cgaggtgggc ggatcacgag      840
gtcaggagat cgagaccatc ctggccaaca cagtgaaacc ctgtctccac taaaaaacac      900
aaaaaattas ccaggtgttt ggtggcgggc acctgcagtc ccagctastc aggagtctga      960
ggcaggagaa tggcatgaac ccgggaggcg gagcttgcag tgagccaaga tggcgccact     1020
gagctccagc ctgggcaaca gagcgagact atgtctcaaa atagtaataa taataatttt     1080
aaaataaggg ggaaaaaatc actgataaac caaaaacctc aaccttaaga aacgttcaca     1140
tctgtatagc taatactctg acgatgggga tacaaaaaca ccttcactca gtggtcttgc     1200
agatatcatt ttttcccag tatttttggg aaagaaccaa tctttgtctt ttttctcct      1260
tcttcaggga actttatgaa tccagaaaga gccaacgttt gaatgattac tgcaatctca     1320
catctattaa atcctgatac ctgcaaccaa gagatgagta ggagatgtgg atcctaagag     1380
gtgacctgta acatactgcc ccct                                            1404


<210> 114
<211> 853
<212> DNA
<213> Homo sapiens

<400> 114
gggtcgaccc acgcgtccgg gtgaattaac acgtacccaa tggccaagag tagatttggg       60
tgtcagtgat aaaatttca ttttcaaaaa cctggtgttc tcagttacag ctttatataa       120
gtatagtaat aactttagca gagctgtaga gagatagatt tgcaaacttg aagtgatatg      180
ggataaatct ccatacgtgg tagaatttta tataaaatgg catatttcaa ggtatgtgtg      240
attatttggt ttcagcaatt ctgtgttgaa gaaactagta tcataaaaaa tgttcgtatg      300
ctgacatcag aattccagaa ttcatatgcc acccctgttt ctgggctcct tcctggtgct      360
gtggcttgga ggggtggtgc tgtgtacggg tgggtgaggc acgccatgca ggtattgcag      420
aaggaaccca cgcaaccgtc atcctttcta cccccaagtg atgctgcctc attctggggt      480
cctgaaagta ggcttcactt aacatggtag ggaagtttct ggctgaaaaa gcaaaaggct      540
tttatcactg gagtctatcc tgagcccccc gtgcaaaagg cagtgtgaac tcaggggaca      600
gaatcactga agcttttgta aaagcacaac atctgcctat cacagtccaa aggggacttc      660
aaaatcaaga atgtctgtga cggagaagat ggaaacagag cctggctgat ggttgtaggt      720
gaatcttctc tgtgtcgaga tgttatcagt gaccgttttc tttatttcat gaagaaacat      780
ttttaatata ttcacctccc tgcatatatt ctgtttactg tgttattgtt aaaaaaaaaa      840
aaaaagggcg gcc                                                        853


<210> 115
<211> 845
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (845)
<223> n equals a,t,g, or c

<400> 115
aactagtgga tcccccgggc tgcaggaatt cggcacgaat ggatctgtgt ggatggtgtg       60
tgccctgggt gtgtatgtmt gtrtgtctgc acccactgca gcagtaccca agcctgccaa      120
gggcaccatt tgcttgaaga tgctttctgg tgccaactgt gcctgccaag gacaggtgac      180
cagacagcat tagacaggct gtgacctgaa caggcacggc cagagccaag ggggctgctg      240
cagctccttc tccagctgtc actgctccca gcccttcctg ccccctctcc tggcacatcc      300
cccaaggcct tcaggctgac ccctggattt cagaacaccc ctcttcatca gaacgtatcc      360
agcctgggtt ccatgcccat caacagcaag acaccagttc ccctgcataa acaggtgctg      420
aagtcaggag gactcaggca gacacactgt acacatcacc gcaagctctc cttcagtcct      480
cccaacgact wtaagtgagg tgttaatatg cctgttttac agataaggta actgaggatc      540
aagaagttaa gtgatttgtt caaggttgtc actgcagcag ttttgtggtt tcctctctaa      600
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gatggagaga agttacacca ggacttagtg cctgggaagc aaagaggtga aattactcgg 660
ccaggattgc acagctgaca gtgatgatac cgatggctgt gcttttagta gctgttaggt 720
accaggaact gtgcttggcc cttgacacat ataatttcac ggaatcctca cagcagatta 780
aaaaaaaaaa aaggtaccat attgtcccca ttttacagac caccccttac aagagtggga 840
tggtn 845

<210> 116
<211> 760
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (13)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (300)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (425)
<223> n equals a,t,g, or c

<400> 116
cggacgcgtg ggncggacgc gtggggaaaa aataacaaaa caaaaaacaa gaaaaaaaaa 60
acacaaaacc ccgtaaaatc acaaagaaaa tccaacacca aaggcgcaga agccggctgg 120
ccgtggtggg ggcagcgtag gcgtasatcc ctctcctctc acttagcctg ttgactcttg 180
ttattatcat gatattcaca aaacgccgca tgtttaaaaa gtcatagatg tcatcttctc 240
tctgccccca gggaggaaag ccacctttct ttgccccttg gccccttgt caggggccan 300
gggtctgccg ggtgggggtg ccaacaggcc tggccctttc ctcccctgca tccagccatg 360
ggggcctctg cgattgccgg aaggttgcat ggctggtccc agggccagca caggcccgag 420
gccgngctgc ctggttttat ttttatttaa ctttattttc tgttttatga gtgtgtgtcc 480
gcccaccccc acccccttca gtgttaagtg gggagccctg ggggagtctc tcctgcctcc 540
cagcctctcc caagacctcc cccctcgtca ccagccatcc ctctggacca ggcagagggc 600
ggaccgggtg ggcaggggcc tgagggtggc tcgggccagc ccaccagcca atggacccct 660
cctcaggccg ccagtgtcgc cctgcccctt tttaaaacaa aatgccctcg tttgtaaacc 720
cttagacgct tgagaataaa ccccttcctt ttcttccaaa 760

<210> 117
<211> 988
<212> DNA
<213> Homo sapiens

<400> 117
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atcttgcacg tctggtcggc tcctgctccc tccttctgct actgggggcc ctgtctggat 120
gggcggccag cgatgacccc attgagaagg tcattgaagg gatcaaccga gggctgagca 180
atgcagagag agaggtgggc aaggccctgg atggcatcaa cagtggaatc acgcatgccg 240
gaagggaagt ggagaaggtt ttcaacggac ttagcaacat ggggagccac accggcaagg 300
agttggacaa aggcgtccag gggctcaacc acggcatgga caaggttgcc catgagatca 360
accatggtat tggacaagca ggaaaggaag cagagaagct tggccatggg gtcaacaacg 420
ctgctggaca ggccgggaag gaagcagaca aagcggtcca agggttccac actggggtcc 480
accaggctgg gaaggaagca gagaaacttg gccaaggggt caaccatgct gctgaccagg 540

ctggaaagga aktggagaag cttggcccaa gtgcccacca tgctgctggc caggccggga 600
aggagctgca gaatgctcat aatggggtca accaagccag caaggaggcc aaccagctgc 660
tgaatggcaa ccatcaaagc ggatcttcca gccatcaagg aggggccaca accacgccgt 720
tagcctctgg ggcctcggtc aacacgcctt tcatcaacct tcccgccctg tggaggagcg 780
tcgccaacat catgccctaa actggcatcc ggccttgctg ggagaataat gtcgccgttg 840
tcacatcagc tgacatgacc tggaggggtt gggggtgggg gacaggtttc tgaaatccct 900
gaaggggggtt gtactgggat ttgtgaataa acttgataca ctaaaaaaaa aaaaaaaaaa 960
aaaaaaaaaa aaaaaaagag gaggggggg 988

<210> 118
<211> 1947
<212> DNA
<213> Homo sapiens

<400> 118
gaattcggca cgagttgtgg tctatttaat gccatgcttt tcctgttttt gtactgtttg 60
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cacaagtcca agaaatattt atgtaaagtg aaagctgcct gcaagattca agcctggtat 180
agatgttgga gagcacacaa agaatatcta gctatattaa aagctgttaa aattattcaa 240
ggttgcttct ataccaaact agagagaaca cggtttttga atgtgagagc atcagcaatt 300
atcattcaga gaaaatggag agctatactt cctgcaaaga tagctcatga acacttctta 360
atgataaaaa gacatcgagc tgcttgtttg atccaagcac attatagagg atataaagga 420
aggcaggtct ttcttcggca gaaatctgct gctttgatca tacaaaaata tatacgagcc 480
agggaggcyg gaaagcmtga aaggataaaa tatattgaat ttaaaaatct acagttatcc 540
tacaagcayt ggtgcgtggt tggytagtac gaaaaagatt tttagaacag agagccaaaa 600
ttscgacttc cttccacttc actgcagctg catattatca cctgaatgct gttagaattc 660
aaagagccta taaactttac ctggctgtga agaatgctaa caagcaggtt aattcagtca 720
tctgtattca gagatggttt cgagcaagat tacaagaaaa gagatttatt cagaaatatc 780
atagcatcaa aaagattgag catgaaggtc aagaatgtct gagccagcga aatagggctg 840
catcagtaat acagaaagca gtgcgccatt ttctcctccg taaaaagcag gaaaaattca 900
ctagtggaat cattaaaatt caggcattat ggagaggcta ttcttggagg aagaaaaatg 960
attgtacaaa aattaaagct atacgactaa gtcttcaagt tgttaatagg gagattcgag 1020
aagaaaacaa actctacaaa agaactgcac ttgcacttca ttacctttg acatataagc 1080
acctttctgc cattcttgag gccttaaaac acctagaggt agttactaga ttgtctccac 1140
tttgttgtga gaacatggcc cagagtggag caatttctaa aatattkgtt ttgatccgaa 1200
gttgtaatcg cagtattcct tgtatggaag tcatcagata tgctgtgcaa gtcttgctta 1260
atgtatctaa gtatgagaaa actacttcag cagtttatga tgtagaaaat tgtatagata 1320
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gcggaagcat ttttacaaaa acttgttgtt tgttggctat tttactgaag acaacaaata 1440
gagcctctga tgtacgaagt aggtccaaag ttgttgaccg tatttacagt ctctacaaac 1500
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cttctataag cattcctttt atcccagaaa cacctgtaag gaccagaata gtttcaagac 1620
ttaagccaga ttgggttttg agaagagata acatggaaga aatcacaaat cccctgcaag 1680
ctattcaaat ggtgatggat acgcttggca ttccttatta gtaaatgtwa acatttttcag 1740
tatgtatagt gtwaagaaat attaaagcca atcatgagta cgtaaagtga tttttgctct 1800
ctgtgtwcaa cttttaaaat ctgactttgt tttaaaaaaa cataaactgt tcattacatt 1860
cttcattttt atcatttata gttttatgca tgtaataaac taatatgtca taagatgaaa 1920
aaaaaaaaaa aaaaaaaaaa aactcga 1947

<210> 119
<211> 1448
<212> DNA
<213> Homo sapiens

<220>
<221> SITE

<222> (1441)
<223> n equals a,t,g, or c

<400> 119
tcgacccacg cgtccggaac gtgctccgcg ggctcagtcc gcccgccgct gcgtccgcgg 60
agtgcaagtg agcttctcgg ctgccccgcg ggccgggggtg cggagccgac atgcgcccgc 120
ttctcggcct ccttctggtc ttcgccggct gcaccttcgc cttgtacttg ctgtcgacgc 180
gactgccccg cgggcggaga ctgggctcca ccgaggaggc tggaggcagg tgctgtggt 240
tcccctccga cctggcagag ctgcgggagc tctctgaggt ccttcgagag taccggaagg 300
agcaccaggc ctacgtgttc ctgctcttct gcggcgccta cctctaacaa acaaggcttt 360
gccatccccg gttccagttt cctgaatgtt ttagctggtg ccttgtttgg gccatggctg 420
gggcttctgc tgtgctgtgt gttgacctcg gtgggtgcca catgctgcta cctgctctcc 480
agtatttttg gcaaacagtt ggtggtgtcc tacttttcctg ataaagtggc cctgctgcag 540
agaaaggtgg aggagaacag aaacagcttg ttttttttct tattgttttt gagacttttc 600
cccatgacac caaactggtt cttgaacctc tcggccccaa ttctgaacat tcccatcgtg 660
cagttcttct tctcagttct tatcggtttg atcccatata atttcatctg tgtgcagaca 720
gggtccatcc tgtcaaccct aacctctctg gatgctcttt tctcctggga cactgtcttt 780
aagctgttgg ccattgccat ggtggcatta attcctggaa ccctcattaa aaaatttagt 840
cagaaacatc tgcaattgaa tgaaacaagt actgctaatc atatacacag tagaaaagac 900
acatgatctg gatttctgt ttgccacatc cctgggactc agttgcttat ttgtgtaatg 960
gatgtggtcc tctaaagccc ctcattgttt ttgattgcct tctataggtg atgtggacac 1020
tgtgcatcaa tgtgcagtgt cttttcagaa aggacactct gctcttgaag gtgtattaca 1080
tcaggttttc aaaccagccc tggtgtagca gacactgcaa cagatgcctc ctagaaaatg 1140
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ccggtgattc acaagtcagg agttcaagac cagcctggcc aagatggtga aatcctgtct 1260
ctaataaaaa tacaaaaatt agccaggcgt ggtggcaggc acctgtaatc ccagctactc 1320
gggaggctga ggcaggagaa ttgcttgaac caaggtggca gaggttgcag taagccaaga 1380
tcacaccact gcactccagc ctgggtgata gagtgagaca ctgtcttgac aaaaaaaaaa 1440
naaaaaaa 1448

<210> 120
<211> 496
<212> DNA
<213> Homo sapiens

<400> 120
tcgacccacg cgtccgaact gacacaatga aactgtcagg catgtttctg ctcctctctc 60
tggctctttt ctgcttttta acaggtgtct tcagtcaggg aggacaggtt gactgtggtg 120
agttccagga caccaaggtc tactgcactc gggaatctaa cccacactgt ggctctgatg 180
gccagacata tggcaataaa tgtgcctttct gtaaggccat agtgaaaagt ggtggaaaga 240
ttagcctaaa gcatcctgga aaatgctgag ttaaagccaa tgtttcttgg tgacttgcca 300
gcttttgcag ccttcttttc tcacttctgc ttatactttt gctggtggat tcctttaatt 360
cataaagaca tacctactct gcctgggtct tgaggagttc aatgtatgtc tatttctctt 420
gattcacttg tcaataaagt acattctgca aaagcaaaaa aaaaaaaaaa aaaaaaaaaa 480
aaaaaaaaaa aaaaaa 496

<210> 121
<211> 1174
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (1151)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (1160)
<223> n equals a,t,g, or c

<400> 121
gagaggttca ggttggtctt gctggcatct tcacctaaaa tagggtctgg cagacaggcc 60
catgcgctgc atcctgccca cggcctgata gatggcctgt gaatggcttt tttacatttt 120
aaaagtggtt gaaaacaaat taaaaatata tttcatgaca tgaaaatcat gaaattcaca 180
tttcattatc tgagaataaa cttttatgga tgcagccatg cctgtctgtc catgtcttat 240
ctgtgtctgc tttgtgctac ggctgcagag tggagtggct gggactgaga cggaacgccc 300
tcctcacggg gccgcgtctc tccaccagga ccgcgggggct actctgaggc tctgctttt 360
ccccagcggg gttggcttcc tgctattcct cagtatcctg ccttggtcct gagttggtcc 420
ctctgscaag agccgtttct gtgtctcagt ggatggcgca ctgsccttct tgttggtacc 480
ttgactgata gackggttcc tgttcackgc yccgaagtca tcccagaaaa cctctyacag 540
ttgcatgggt tgaacccagt ccgcgtgtat ttagagtttt gtctcttgcc ccttcaccca 600
gaacagcagc acccaccacc ttcctgtccc ctgtgactgc ctcgcaactg ggtctgttct 660
gtgagatgtc gccaccctgt ttgccatctg ggaggatctc actccttcaa tttaatctgc 720
tctcttccgt tatttttta gtttctatgt attttacttt taggacattc cagcctgggt 780
gacagagtga cggtctcaaa aaaaaaaaaa aaaaaaaaag cacaccagtg tcttccattt 840
ctcttttaat cataatcatg ctttaaaaaa taccctcgag catatggagc aaatttaaga 900
taattgttcc ttttctgcta attcattatt actgtcatat ctaggtctgt ttctgtcgac 960
tgtggaccac ttatgtgcga tccgtggacc acttgcgtgc gatctgtcgg ccgacgatga 1020
gcttgttcgg atgtagctcc atcgtaagtc gaggagcatc tgtgatttgt cctctgctta 1080
tgggatatgt ttttccgcta ctragtctgt gtagtaaatt tttgactagg aaaaaaaaaa 1140
aaaaaaaact nggggggggn ccccgtaacc catt 1174

<210> 122
<211> 1046
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (14)
<223> n equals a,t,g, or c

<400> 122
ttgcaggaat tcgncacgag cactagtagc tggtgytcca ggctggcggc gctcaccttt 60
ctcctagccg ggtgacccag gggatttatt ttatgttggc tttctctgaa atgccaaagc 120
cacccgatta ttcagagctg agtgactctt taacgcttgc cgtgggaaca ggaagatttt 180
cgggaccatt gcacagagca tggagaatga tgaacttccg tcagcggatg ggatggattg 240
gagtgggatt gtatctgtta gccagtgcag cagcatttta ctatgttttt gaaatcagtg 300
agacttacaa caggctggcc ttggaacaca ttcaacagca ccctgaggag ccccttgaag 360
gaaccacatg gacacactcc ttgaaagctc aattactctc cttgcctttt tgggtgtgga 420
cagttatttt tctggtacct tacttacaga tgtttttgtt cctatactct tgtacaagag 480
ctgatcccaa aacagtgggc tactgtatca tccctatatg cttggcagtt atttgcaatc 540
gccaccaggc atttgtcaag gcttctaatc agatcagcag actacaactg attgacacgt 600
aaaatcagtc accgtttttt ccctacgatt acaaaactgc cagtcctata tggagtctga 660
tcacaagact gcagtttctt cacagatctc aggaagttgt cgtggggcag aggctttta 720
aaaacatgtg attagggagc tatctttatc tgaataataa cgaattttta ggtaaaacct 780
gagatagagt actacaaaat catgttgatg acttcagatt ttggaagtta aatcatgtct 840
gttatttgca ttctttagaa acttgactaa gtacctgaat tcatatttct attctactgt 900
gcaacatagt gatgattcag aaatttttcc tttggggaaa aaaatgaata tgaacatttc 960
cattgtgtta agtgtaaaaa ggtccagaca tgatcataaa atttaaattt tatacaaawa 1020
aaaaaaaaaa aaaaaaaaac tcgtag 1046

<210> 123
<211> 1160
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (325)
<223> n equals a,t,g, or c

<400> 123
ggtcctatgt gtctataact tatcagattg ggagctagca gaaagagata agattattgc 60
tatataattt ttagggatag acaatttaat ttccttggtt tcctgtctca tggacctcac 120
ttaaccagta gtatgtgggt gtttttttcta ccttttttct ccatcttatt taaaatttgt 180
tggtgtattt cccttagtca aactaaagag aaacaatcat ctaatcttat gttttatttc 240
ttttgtatat gtacatatga gaggaggagg aagaaagaga tgaggagagg tgaaaagaaa 300
agatcccttct gcctgattgg gcttngccag catatgatag cagtgcaggc ctggttccat 360
gagcagcatc agattcaaat ttcatagaaa aagagcccag aggaattgaa aaagagaaat 420
taaattcaac aaggagaggc attgtataca ttatgcattc acgataggtt atgattgaga 480
agaagctggt gctttgggaa aaacatatta ggttctacat ttacccttct tgaatagttt 540
tctcctttct aaacagggtg ataataggag aatgctgaat gcctctccat tgaatttgga 600
aactgccggg ccagcattag tgtggtattg tctgcccaca cttttctaga tgcaagttta 660
agatcatgtt cagtgtgaac attgaggact ttagagatcg gagtccgaaa tgtgtcaaag 720
ttaatgttaa tagatgctgt cctcattttg taactgtgac ttctaaatgt gacctttag 780
ttcatatctc ataaatttgc catttaagaa gaaatacaga watgaaagtt tkaagtttta 840
ataaaagtat atcttgctgg gtgcagtggc tcatgcctat aatcccagca ctttgggagg 900
ccaaggccgg cagatcactt gaggtcagga rttggaract agcctggcca acatggcaaa 960
accttgtccc tactaaagat acaaaaaaaa taggtgggca tggtggtgca catccgtatt 1020
cctagctact tggaaggctg aggcacaaga atcgcttgaa cccgggagac agaggttgca 1080
gtgagccgtg attgcaccag tgcactccaa cctgggtgac acagtgagac tgattcaaaa 1140
aaaaaaaaaa aaaactcgag 1160

<210> 124
<211> 893
<212> DNA
<213> Homo sapiens

<400> 124
ggcacgagta agggataaag tgggcctgag cccagtacat cctctgcagg aggctgaagt 60
ttctgaaaca agaagtggga gagggttcag taggaaggtc cacaagtgag gtcgaccaaa 120
gagatcctgc tgtttcccca tgagtgccac aagggactgg ggtggaaggg ctgaggctgg 180
accagtcctg gatgcagtgg ccttttctgt gtgttcttcc tctgctccct caggtctgga 240
gggctgggag cctgctgcgt gctctggaac tttactcagt cttgttgagc cactttcttt 300
gggaaatgtg gaccatgtct cttaaagaac cagaattgct tctttccacc aagtcattaa 360
ctgtgtggag arggagagag cccctgtcag aaattgggggg atgcagactg aacaatgaag 420
gaacatagca acaatgaagg aacataggga caatgacwcc accttgagtc cagtggaatg 480
aggtgcggct gcattaaaga atgaggaamg ggacagagac aggtgtaaga gacgatggaa 540
caatcascca agaaagtcag ggggttggct gggcgcggtg gctcacacct gtaatcgccg 600
cactttggga ggctgtggcg ggcagatggc ttaagcccag gagttcgaga ccagcctgaa 660
caacatggca aaaccccatc tctacgaaaa atgcaaaaat tagccaggca tggtggcatg 720
cccatgcagt ctcagctact tgggaagctg aggtgggagg atggcttgag cctggcaggc 780
agaagttgca gtgagacaag atttttaaa aggccaggca tggtggctaa tgcctgtaat 840
ctcagcactt tgggaggcca aggtaggcgg atcacctgag gtcaggagct cga 893

<210> 125

<211> 1049
<212> DNA
<213> Homo sapiens

<400> 125
ggcacaggaa aaagccatct aaggtgctaa gttaaaagaa aaaaaaaagg ccttataagg 60
tactcaggat ctacacgagg ttgttaattc atgttttgct ttaattggtt actctgtttc 120
ctatttcctc ggtttccaat acttgtttgt agaaaaacatc agttttgtgt gtatttgctc 180
ttggtcctaa agttaaggac actatacgca gagttaattg accttcattt gtgtgccagc 240
attctggggt gacataatgc ctgcaagtgt catattctta atatgtgagg gggttctata 300
tggagtacag ggttagttgc taaataacct ctgtaccccct ttttctctgt ctcgatgtat 360
gcatctcatc tcctgtagat tgcctatttg tatgtattcc tagaaaaggc cttcgatagg 420
acgtctgtag ggktattccc ttctaaaggg aatggttata ccctctgacc tatcaattcc 480
atttctataa atttatccca tagatatact cacaaatgtg taaaatgaag tatatttgaa 540
gtaaattatt aaagcmttaa gagcaagcta aatgttcatc agcaggaaat ggagtcaata 600
tatcttcgtc tgtctgtata atggaacaat atgtattatt atgaacagtt tttgagcaaa 660
taaaaataag ctgaagttta aaaagttgag ttaaaaaagc aaggtgtaaa acagtatgcg 720
tagtatctgt gtacgtttgt agatactgta cacacatgtt agagggcaat ttggataaag 780
tattctgtgc tcaattaaca tatttcccct ttgtcttcct ggctctactg gcttattacc 840
agtagcagtt actcgggagt tacccagcta ctcaggaggc tgaggcagga gaatcgcttg 900
aacccaggag gtggaggttg cagtgagctg agatcgcgcc tgggtgacag aacaagactc 960
cgtctcaaga aaaaaaaatg cttatgttct gtataaaatc ttcaawaaaa tgacgatacc 1020
agtaaaaaaa aaaaaaaaaa acctccgta 1049

<210> 126
<211> 1626
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (525)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (542)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (562)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (607)
<223> n equals a,t,g, or c

<400> 126
ccacgcgtcc gacgcggcgc acgcggcagt cctgatggcc cggcatgggt taccgctgct 60
gcccctgctg tcgctcctgg tcggcgcgtg gctcaagcta ggaaatggac aggctactag 120
catggtccaa ctgcagggtg ggagattcct gatgggaaca aattctccag acagcagaga 180
tggtgaaggg cctgtgcggg aggcgacagt gaaacccttt gccatcgaca tatttcctgt 240
caccaacaaa gatttcaggg attttgtcag ggagaaaaag tatcggacag aagctgagat 300
gtttggatgg agctttgtct ttgaggactt tgtctctgat gagctgagaa acaaagccac 360
ccagccaatg aagtctgtac tctggtggct tccagtggaa aaggcatttt ggaggcagcc 420

tgcaggtcct ggctctggca tccgagagag actggagcac ccagtgttac acgtgagctg 480
gratgacgcc cgtgcctaat gtgcytkgsg ggggraaacg actgncccac sggagggaag 540
antggggagt ttttccgccc gnaggggggc ttgaarggtc caagtttacc ccatgggggg 600
aactggnttc cagccaaacc gcaccaacct gtggcaggga aagttcccca agggagacaa 660
agctgaggat ggcttccatg gagtctcccc agtgaatgct ttccccgccc agaacaacta 720
cgggctctat gacctcctgg ggaacgtgtg ggagtggaca gcatcaccgt accaggctgc 780
tgagcaggac atgcgcgtcc tccggggggc atcctggatc gacacagctg atggctctgc 840
caatcaccgg gcccgggtca ccaccaggat gggcaacact ccagattcag cctcagacaa 900
cctcggtttc cgctgtgctg cagacgcagg ccggccgcca ggggagctgt aagcagccgg 960
gtggtgacaa ggagaaaagc cttctagggt cactgtcatt ccctggccat gttgcaaaca 1020
gcgcaattcc aagctcgaga gcttcagcct caggaaagaa cttccccttc cctgtctccc 1080
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ggtctgggag aaccagatga tgtactaggt gaagcattgc attgtgggaa tcacaaagca 1560
aatagtactc cagaaagacc ctgtctcaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1620
aaaaaa 1626

<210> 127
<211> 1177
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (484)
<223> n equals a,t,g, or c

<400> 127
ccacgcgtcc gctatcatca gagcatgtca cagatctatg gactcattca tggtgacctg 60
tgttttattc caaacgtcta tgctgctttg ttcactgcag ctcttgttcc tttgacgtgc 120
ctcgtggtgg tgttcgtggt gttcatccat gcctaccagg tgaagccaca gtggaaagca 180
tatgatgatg tcttcagagg aaggacaaat gctgcagaaa ttccactgat tttatatctc 240
tttgctctga tttccgtgac atggctttgg ggaggactac acatggccta cagacacttc 300
tggatgttgg ttctctttgt cattttcaac agtctgcagg gactttatgt tttcatggtt 360
tatttcattt tacacaacca aatgtgttgc cctatgaagg ccagttacac tgtggaaatg 420
aatgggcatc ctggacccag cacagccttt ttcacgcccg ggagtggaat gcctcctgct 480
ggangggaaa tcagcaagtc cacccagaat ctcaatcggt ggtatggagg aaggtgccac 540
ctgactggga gagagcatcc ttccaaacag gggartcaag gccagcccyg rwttaaagcc 600
aagtccacaa aatggrgcca cgktcccgtc ctctggagga tatggccagg grtcactgat 660
agccgatgag gagtcccagg agtttgatga tttaatattt gcattaaaaa ctggtgctgg 720
tctcagtgtc agtgataatg aatctggtca aggcagccag gagggggca cccttgactg 780
actccccaga tcgtggagct ccaggaggat acccatcgcc gacactcacc tgtagcacct 840
cactaaccat tcgactgagc acactttcat atttgtatca gcttttgtgc taaaactctc 900
taagtacatc cacctgtgta ataggaacct gtgaattgta ctggatgatt aatacaaacg 960
tgattgttgt atttggagta taaattactg attgtatgtg acctgaaaat tcactgctat 1020
aagaaaggtg gagtcagttt gtatcagtta ataggatgtt catattccaa ggatattagt 1080
tgtttttta atcatcctat atggctaaca ttgtttaatg aaagtaataa tcaataaagc 1140
aatagaatct aaaaaaaaaa aaaaaaaaaa aaaaaaa 1177

<210> 128
<211> 1276

<212> DNA
<213> Homo sapiens

<400> 128
tcgacccacg cgtccgccca cgcgtccgct taatatctgt attcccagtt gcctacggga 60
taaaagccca aactccttag cagagaatat aaggccctag ctcccacatt atttcagcag 120
tcatcaccca ctatgttcct caagactgca gccattaact ttttagagtt ccctaaacat 180
gctgtttact ttcatgcctc tatcccgttg tctgtggaat gacttccctc cttgccctt 240
tcagtgctac aaaccccta tctttaagac atagtacaaa tggcatctcc tggttggcat 300
ctttcctgca ggcctacagg cctagtaagt atcttcctcc tctgtgctcc tgcatacctc 360
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ctcaggcata gaactcattt cctttatggy tctataatgg aactttaccc aactctcacg 480
ttccccatga ccacagatgt ggaaaatttg aatcttgaca gttcaaggtg aactcagtca 540
ttttcagagt tttcatagtc ccttcaagat tgaaactcag ttcctgcaat gtttgcccct 600
tttctcctct tttgtctatg ctgggagagg cattgtgggg agggttgtct ggcttatggc 660
tcccattgtc ctctgcttga taaaccacct gagctttggt cattagcagt ctcctgtgcc 720
tttcacactc aggtagtgtc tgcacaggcc actctatgtc ttttccatgc tgaagaaatt 780
cctttccagg ccatgtctgt gttcctcctg ccacacagga aatttttgag catgttcatc 840
ctccaagctg aatgcagggt cttgggtagt ggtcctcacc tgctccagag acttctccag 900
ccattgccac tctccactca ggtgatgaag ctggatgagg gactgcaccc accagagtca 960
ggccagggtc ctgtctgctc tgtgagtccc tccaattgtt cttattccga gatttccatt 1020
gttctgcccc ctcttgactc ccagggctct caagggagtg ggggtagtga agggagccct 1080
ttcccaagct cccccaagag ctctagtcac atcacttctg atacttcttt tcccaccagc 1140
tggaagaaag aactttcatt tgtcttgaaa tgagaaaaat gttcttagaa tattttgtat 1200
tactctctgc tctgtcattt atggtaaaca aaataaaata ataaaaaaaa aaaaaaaaaa 1260
aaaaaaaagg gcggcc 1276

<210> 129
<211> 1334
<212> DNA
<213> Homo sapiens

<400> 129
tctcagtggt cagaggctgt gttggaccca tagtagaatt ttccagtcac agacccaagc 60
ttccatgggt tgttactgtg ctgtaccact tggtggktct gattctgaac ctgatgtgtg 120
tgttaattat attttaagca acacacacac acacacacgc ctcatgtaat ggacttttat 180
aacaaaagaa aaaatttgga tttctaattt acaaatggca aattatttat ccctctctgg 240
atgcaccaaa gaccagtaaa gtttatagct tttccatcta tatttataaa gcaatacttgt 300
attataaaaa tcaatatttt tatcacatgc ttgaaatttt tattttgttg ttttaaaatg 360
tgcactctaa acatatcaga accttatttc ttcctatgaa cttaagctgc ctgcgcacaa 420
aaaaaaaaaa aatttaccaa atggagatgc agtagagtcc ataggctcta aaaactaaaa 480
gaaatgggat gcaggggggaa caagttattt gtcctgagtt actgtacttg cttgacatgg 540
ttgttgggta ctaaatcaca aaagaatcca ttccaggtat gcatgtctgg gggttgggct 600
gtgtctagat tagaaactgg gtttcaagct ttgcatgatg ggagagcgtc ctctcctcta 660
tcagctgcgt gtgttctgga taggacagta gcccggagat ggaaaccacc ttcagtacca 720
ttagcccacc ataccaagta acaagttagg caggaatcgt gggaatttat tgagtcagct 780
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tgagttcatg gttctttagg tcaccttaat accagctatc tttggtagaa gctacagcat 900
tcagtttctc tggaaactgt atcacatttt tgcattttaa aaattttaca gtatcaaaaa 960
accaaaatct gcttatgaaa caaaacatga agcaggacat atttggattc tatttattta 1020
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actgttagca ggtagtttgt ggcaaagatg gctaaataat gaagcaaatt agaatctgtg 1140
tgtatactaa tgagctgctt tttttctgtt gagactatca ttatttgtct tattacccaa 1200
gaggcaatta cctgaatttg gatgtctgaa ttataactta tgcaggaata gttctgtaaa 1260
tacatttaaa taaactgtaa agatatttaa taaatatagt atttatacta aaaaaaaaaa 1320
aaaaaaaact cgag 1334

<210> 130
<211> 532
<212> DNA
<213> Homo sapiens

<400> 130
ggcacgagcc ttgggccatc tcctaaaatg atctttatca taatagctac agtaaaaaga 60
aagaaggaga ggtattaatg tgggtggaaa tcaggacagt ttcctaatgc cgtggcttac 120
aattctgaga tttctccagg catcaggaca tgtgcgcgca caggacttgg ctctcttagg 180
agatacttca gtttgtatca gatgtggctg tggagggtgc tctttaagca ttgctaacta 240
tgagtgggtc cctcttcagaa ggaaggactg taagaggtat gaaacttctg agaaaacgag 300
ctgtctttctc ttaccaagcg cctgcagccg tcaaaatgct gtaggcttta gtcgtctgcc 360
agttcccaag ctgagctgtc tccttcatgg ataggatttg tttgtttaga aacaacaaca 420
aagttcattc tgtttataac tcagagcatt tgtttttttct gctgaggcta aaatacttgt 480
ttattctttc ctagaggaga aaagaaaaaa aaaaaaaaaa aaaaaaaaaa aa 532

<210> 131
<211> 685
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (491)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (661)
<223> n equals a,t,g, or c

<400> 131
tcgctctctt tctttctctt cttctctctg tttttaagtc aagtattggt caaaaaaatg 60
caatcttctg ttttttgttc agcagacaat cattttcttc gtaagcacct ttttctctcc 120
actctgtcac tgcctgtgtg ggtactggtt ataaatgtgg aaaaagaata gttatgactg 180
taacagattt ttatttttat ttcaaaattt tatatgaatt atgtatatct taatgatcgg 240
tcatttttccc agtttgtaat atatgtgtag aaattgcctg tatatgatat tgctttttct 300
cctctccctt tctctttctc tcctctccct ctctctgtct ttctccccgc tcaactgtct 360
cttttctttt tggggttctc ctcccactcg gtgctcctgg tgtcgacttg gcagtcaagg 420
agaggcatgg tggcctgggt taggaagagg gaccctgtcg ctagcaaaag cggagagtga 480
gattgtagta ntcttatgca aaagctattt ccagtatttc ttagcagctt cagaggtatc 540
tctcactccc tgtagggcgc ttttactgtt atcttaaact gcgtgtttat ctatatgtaa 600
aaactttcta aagcaaatac agtattctcc attttcttat caaaaaaaaa aaaaaaaaac 660
ncgaggggggg gccgtaccat tcgcc 685

<210> 132
<211> 729
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (725)
<223> n equals a,t,g, or c

<400> 132
tcgacccacg cgtccggcca tttagaaata atcaactctt aatcagcctg ggatagtcag 60
tactaaaagc accttcatga gctgtgaaaa atttaatgca tttatttaca tatttagttt 120
taaattttag tatattgtta gttgaggtat agtttccaaa caaagagccg tgaaatgttt 180
agtaactgtc tctgtacctc tggatgagga cagctcagcc gggaatggag ggggactggg 240
tgaggagacc agaatgtcag tgtggccacg cagcacactt ttgttttgtc ttctgtcctt 300
gagcactggc ttgttcctgg ataaactagg cataataata cctatcctgc tgtgtgggtg 360
gaagttaaat gtgataatga tgtgtgtgag atgcctgcac agtgcctgga ggtattgaag 420
aattattgct gcctwttctt tttctaccta ccacttaccc gctacccccg ggtgctacat 480
gttagaaaac actgtgtaaa gtgtggatgc ttctgaaaaa tctcccctgcc agcagttagt 540
gccaatagcg tgcagaaaat aagatgcaat gatttggctt cttttctgtt tggcaataag 600
aagcttattt gcmcatagcc tgatttcttt caatctgcaa aaaaaaaaaa aaaaaaaaaa 660
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 720
rgggnggcc 729

<210> 133
<211> 1079
<212> DNA
<213> Homo sapiens

<400> 133
ggcacgaggt gttagaaagt tttcgaagca gtgtgagtct tgtacctttg tggtcctgtc 60
tcacagacac ctgtctattc cctgaccctt ttaaatgcta actttctgcc tgtaggaaat 120
cttccctttg tgcttaggtc tttttcttct gtgagcttta gataaacaac ctagtgttta 180
aacttttttaa taagggattc atttttttaat acatgagaat tcatttcaaa attttggttt 240
tagttattta ttttattcta cttggctctt tttcagacag atgttctctc ctggattgta 300
aaagtcgaat tcaaaggatt tttatttgta atatacttaa cctttctctt gtaagttgcc 360
atctgtgtag atacagcttt gattgcctga caagaggaaa atgtttccca ttatcttttc 420
ctgcctgaac tatacggtca cttgtgttcc agcatagtgg ttcttaaccc tcatagtgtg 480
tcagaatcac tttgcagagc ttttaaaaac tctagatgcc tggggaccac cccaaagact 540
ccattttgtt gtcatgggtc aaagcacagt cttctagttt gcagctagtg ttgagtacaa 600
ctagagttta acccagttga attttagttt aatcttggct ggtcttgaag atgttagtaa 660
tctctattca ttttttttkga aaagtaccaa tgaratcaga aagttaatta gaaaacatct 720
agttgaatcc cctgttttta atagatgggg aaaccaagac ccagagaata taatccaaag 780
ctacctgtca cataggccac aatttctttt ccaatattct gttcttcgct gttcttctaa 840
tttgcagaac tcctctttaa aaaaccttg gagaatgtat tggcctcata ccctcttcct 900
tcagcctgaa agacatgcac ctgtcactta tttatgatat ttaaatgcaa cctctagaac 960
aggggtgtcc aatcttctgg cttccctggg ccacattgga agaagaaatg tcctgggcca 1020
cacataaaat acactaatga tagccgatga acttaaaaaa aaaaaaaaaa aaactcgta 1079

<210> 134
<211> 1297
<212> DNA
<213> Homo sapiens

<400> 134
gactcgtgcc gaattcggca cgagggsaag gggcgtcttc tgtccttgtg gtccgcttct 60
aggctttttg gagcatcttc cagggtcact ccagagaccc ccccagacta ctgaatctga 120
atccgttagg tggtccaacc ttcctcttca ggtgtctact agaggcaagg ttggatgtat 180
gcggctgccc tcagtacagc cccttccttg ttttttcttc atttgtgttt acttaaaaca 240
ttaatccttt tctccctctc ctccatccct ctccctcccc tactatacag ttatgactta 300
cactaatcat tcccgatgat ctcccagaag gaaataagtg tctgtctgtc tctgtctctg 360
taccatcgtc ttcttggtac agttcggact atttttttctc tacaccccag ttatgcaaag 420
tgtagtccct gaaccagcag cctcagcatc ctgagggaat ttgttaaaaa cgcgaaatct 480
caagccctac ccagamttac tgaatcagtg tctgcattgc aacaagatcc cctggtaatt 540
cmtatgcaca tcaaaatttg gaaggcacag ctctcaactg atgtcctggg tctccttcac 600

```
atccatcctg ggaaggtctt attcctcatt cctgagctca tcccactgaa gagctatggc      660
acttccaatt cctgagcctt tgtgaggttc tgcgtgtcag taagcttgct tccgggcatc      720
acctccgaaa acacttgggt ttcagttttc tctgtgaggc ttcttaagga gtggaggaaa      780
gtggatgttt tcaagataac gcagctaaca ttcaaagagg ttaagtgaat tgtccaaagt      840
cacacagcaa gcactggaga ggcagtgtct caccatgttg cccggactgg cctcggactt      900
stgggctcgg gccatcctcc cgtctcggcc ttccaagtgc tgagatcgca ggcgtgagcc      960
accacgtccc accgggatac ataggtttta cggtatcctc tgaacctccc tttaatcaag     1020
agagtggaca aaactgtggg tcccycmtyt tcaaaatggc cagtaaaaga ggaaataagg     1080
atatgcaagt ttagttattt tctgctgccc tctttaagtt gattggggat ctctttgtca     1140
ctactttggg aagataactt accttcttat ccactatggc taattggagc ttttctcatg     1200
tctttatggt tgctgggaaa ttttcaaata aaattcactg ggaatggttt gaaattgcaa     1260
aaaaaaaaaa aaaaaaaaaa aaaaaatgac cctcgta                              1297
```

<210> 135
<211> 617
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (9)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (513)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (559)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (587)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (602)
<223> n equals a,t,g, or c

<400> 135

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atggaaaanc aggcaaatcc tgaaatgggc tggaaaaaag ggagggaccc agcactycca       60
gggagaaaac ttggcattyc ttgggaatct aacaggatgc agtgaaccca agccttttga      120
agagctcacc aatcagactg cccttgtcta tccatgagca gatgtttgat agtattgcgg      180
aggccctcta gtgggtatgc tgccaagcaa ctggagtggc acttgggctc taatccagtt      240
gtctatccct ttcaccctgg catttcatca gccaaacaaa aaccaactaa ctcagaaaaa      300
aaggaaagcc cctcaagggt cctttgaccc cgatatctac atagatgcta tcggggtccc      360
ctgaggggta ccaaacraat tcaaagctcg aaatcaaata gctgctggat tcaagtctgt      420
ccttttcttg tggtctacta taaataaaaa tgtagactgg ataaattaca tatactataa      480
aaaaaaaaaa aaaaaaaaaa ctcgaggggg ggnccggtac ccaattcggc ctatagtgag      540
tcgtattaca atcatgggnc gtcgttttac aaagtcgtga ctggggnaaa acctggcgtt      600
anccaattta atcggct                                                    617
```


<210> 136
<211> 1311
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (1284)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (1296)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (1301)
<223> n equals a,t,g, or c

<400> 136

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ggcacagctt ttcaacatgc cttcagcact aatgactgct ccaggaatgt ctacattaag       60
aagaatggct ttactttaca tcgaaacccc attgctcaga gcactgatgg tgcaaggacc      120
aagattggtt tcagtgaggg ccgccatgca tgggaagtgt ggtgggaggg ccctctgggc      180
actgtggcag tgattggaat tgccacaaaa cgggccccca tgcagtgcca aggttatgtg      240
gcattgctgg gcagtgatga ccagagctgg ggctggaatc tggtggacaa taatctacta      300
cataatggag aagtcaatgg cagttttcca cagtgcaaca acgcaccaaa atatcagata      360
ggagaaagaa ttcgagtcat cttggacatg gaagataaga ctttagcttt tgaacgtgga      420
tatgagttcc tgggggttgc ttttagagga cttccaaagg tctgcttata cccagcagtt      480
tctgctgtat atggcaacac agaagtgact ttggtttacc ttggaaaacc tttggacgga      540
tgacagtggc tttyttgtga tgacagacas aatggaggag agatctgctt atgggaagta      600
saaccatgaa gtgactgtca cacatgcatg tccaagaaac atcctgaaaa cacatgaagt      660
cgtaaactgg agaagcagct ctacagcaga gattatctcg tgtttcctct ttctactggg      720
ccagaaaaat cctcagggtt gcagttggtt gagtgggcag ttgacatatg catgttgcac      780
ccgatgttgt ctctaagtta gcaatgtgtt atttccagct ttaaaggtga gattgtagag      840
atgctgtcaa agggataagg aaatagcaag atttttaagt agtgtgtttg tgaagactga      900
tcccatttta caactgcctg ttctttctcc agtccttttt tttccagcca gcttgactat      960
tagaaaagta tgaaactggt tgggttttat ttaatatttt taatatattg agaagcatgg     1020
tctgcctgga ctgcacttct ctaaaagtga gatataaaat tgtgcagcta ttttaaaagt     1080
tgtatataat atgtgtgtaa aaaaaaaaac tgtaaaaaag raaggacaaa caggttgttt     1140
tgttctagtt ctaatttctt aaaaaccact acatggttac aaaattggaa taacattttg     1200
gggggacaac tggggttaac taccaaagaa ggagggattt aaagaggaga tggtggttga     1260
attgacccca tttggaataa tttnaggctt acagtnccca nagctgttag a              1311
```

<210> 137
<211> 1095
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (616)
<223> n equals a,t,g, or c

<400> 137

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gatggtatgt gtgtggtgtg tatagggtga atgtgtggtg tgtgaggtgg gcatggtgtg       60
tgtgaggtgt gtgtggtatg tgtggcatgt gtttggtgtg tatgggaata tactatggat      120
```

```
taggacatgt gggttattca aagatctatc cttttgtgct ttgaaatctg aaatgtagaa      180
actgtggcct cactgaggag gagttttaga atatgcaagg gagatgatca ggactggatc      240
ttgtatttgg gtaccacatc cagtcccaga cagcatgcta aggcaaggag ctcataaaag      300
ccccaagctc tagctgttgg ctacttatct cctggagcat caggtgagcg cgttcaggct      360
ggggagtcct gatggctgcc tggttgttac aggatgttac agcttaggcc tggggacata      420
gcccagcacc ctccagargt tgtgtctgtt ctttactctt caggttccct ggaggcagga      480
gaggarctgg cctcatttct ggcaggcacc ccactactgt tattgagcaa tcctccaggc      540
tgcagagatg tcagaggagg accctaatgt ctcckgattt tgattatttt gttctttttc      600
cctaggtgtt ttactngcag ataccttgag taccttgttt gtatattcac tttgaaagca      660
cacatttaaa tgtttataag gaaaaggttc taaagacatc cattgatcca ttcattcatc      720
attcagcaaa tacctgttga atacctgctg tgtgctaggc actgcggtgg gcgagccaga      780
rggctttgtt gctccaagga rcttgcattc tagtattcta gttattttca cgcatctgca      840
ctatctggga cagggaccat tgcgttttgt cgtatataaa gcagcatgtg tctgcactac      900
agtttgtgtc cgtygcagat gggcaaggat tgagtgcaaa aacttctggg ccaaaagggg      960
ttggcttggg tcaggctgct aagtagctga ggtgaaagca tgtgccaccc ctcctgatac     1020
agggatcctt gctgattgtg tgtgacacca gggccttccc atctgtcagc tgggtttgtc     1080
ctcacagtag ctcga                                                     1095
```

<210> 138
<211> 692
<212> DNA
<213> Homo sapiens

<400> 138

```
ggcacgaggc gaatatgtgt agctcagctg ttttgaaaat gatctgtttg tagaaggcca       60
caaagcaaat attattatct taatcttatt ctgaattttc accactaaaa ccacattcta      120
ttgaaggaat atataataaa agtgcattat catatagtgt cacaatgagg gattcaggtg      180
cgaagggaag actcattcct gtgaaaacat agcccatccc cagcagttgg tagaaggatt      240
tgctggagtt cctcctcttt gtgtggccta taaaacattc catgaggcat gtggcaatag      300
tcacaatgat agtggtctta tctcctccag tcttagcatc ctcactcaag ccacctcttt      360
tcatagacac atactttatg tttgggaaga ggtgctctag gtgggacacc cctgcctgct      420
ccaaataatt cctactgaca tccatggcag cttcattcta tctgagctgg agatttggga      480
atttaggtgg gcacagaaga aagaaggggt ttggggcagt gtcgtttgga tgattttgac      540
agattcttcc tgggggtaaa gagagatagg tgggtctaat catccaggga ataaaatgcm      600
aaggtgtgtg tatatggaaa atccaaggga gaggaaatta aaattatccc agattgctta      660
tttaatagtc aggaaactca actttccatg aa                                    692
```

<210> 139
<211> 748
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (60)
<223> n equals a,t,g, or c

<400> 139

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ggcacgaggt aaggtctgtg ttccacagga cgggacaagg tcttagatgt ttctcaatan       60
ataaggaatg aatctctggg ttggccaatc ccgaactcat tagctctgaa ctcccaacac      120
acattcaggt gcatctgcca tacacggtca ttctcagggt atgctcaagt tattgctatc      180
gggcacatct gccctacaga attccagcag aaatacccaa tgggagtggt gggtctggaa      240
acaggaatgt gggcagagct gaagctgctc tcctgggggа gggctgctat tgctgtgtgg      300
gtgtgcctga gaagagtagt taggggrgga cacagtccac cagcaggtca aggtgggcag      360
ggagttaagg tccagtggga aggagtgcag ggatcaggaa gtggccagcc agaagacatg      420
agatgggaga agctacatgt gaggattctg atgcagggca tgcatggagc cccacaggat      480
```



```
gacatcagat ctgtccacgg ctccacagca tttcctgact gcctccatct accctgcaga      540
cccacctgcc ctgggggttc ctttggatct ggctgaccag atgccccttgt gggagcctgg      600
aggctggagg agagtggatg gtgagaccca ggcctccagc tctcaccctg ccaggccaca      660
gtggtcaggg ctatcaggtt ctaagcccaa actgaggtcc aaggggagtt ggtgggcagg      720
tggcgggtag ctggaaaaca cactcgag                                         748
```

<210> 140
<211> 1132
<212> DNA
<213> Homo sapiens

<400> 140

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ggcacgagca gctaccctta tttgcagaca tcctgagaat gcaatatgat gagcaacttc       60
tgtttcccca atccttgctg aaggtaaata agatttattg ttgccaaaac tcttcaatct      120
acaaaatatt tttttcttta taaaatgctt ttggtctctt gtttcatgtc tatatatttt      180
ctaagccctc ttcttctccc attgcatggc tctcctcacc ctcactctta cctttgtttt      240
gctgtttgca ggacctcctg gtctctgtca gaaaagactt gtaacttccc aaatgaaatg      300
ttgcaacttc ctatttttct gaaatctatt tactaaatgt tatgcaagac atgaaatttt      360
tgcctacttt attccaccat catttgtttt atgaaacaaa caaacaaaaa aatctctaaa      420
cctaacccaa gtagaagatg cttaacttta aggaaacact aggcaacagg cagtatcatg      480
gggtgtcaca ggatatgaac aatggaaagg tctcttggaa ctggaggagg tgctactggg      540
aactagcagt gctctctcca tctctcaggg cccaacccac atggtttcca gtttctttga      600
ttctctctat ctcctctttt attctgctgc tgctgcttgg tcagtcctga atcaaagagc      660
ccttgaaggc cttttcatac catggattag ttaacgaact ttctctctta tagaacatga      720
aggatgtatc actggatagc taattggcca attacctgtc cttgtttaag tatctttgtc      780
aaggtaggca aggaaggcag acaacgctga acgcataggc catgtgatgt ggatcgaata      840
cggcagctgc acaggcctct cccatctcag attgtgaaat gattaattaa tattttcagt      900
tagtaaaaga aactggggtc agcaactcta tgtgtgtgtg tgtgtgtgtg tgtgtatctg      960
tgtgggggtt tatattcaca aatatctgta tatttgatta gaaaacccac agagagatca     1020
agggctctct atatcctgct aagttctgaa ggattccccc ataatgtgcc cccacctact     1080
cactacccta tcctccaatg tcataactgc aatagagatc cacttccatc tg              1132
```

<210> 141
<211> 1112
<212> DNA
<213> Homo sapiens

<400> 141

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gtggcaaatg gggctactcc tgcttttact tcttggttgc tggacccata tatttttttac       60
aaatggaatg atttattggt atcttgaagg ccaccccatt cttaatgaga tcctcttcat      120
tctgcacttt taaagggtat tgcagcactt tatcaggcca gcagctttgg ggtaatactg      180
tatgtggtag gaactgtgga tctttgtggt catatgctgt cattgtacct cctattctgc      240
aaagtggaat ccttgttcta agatactatg tgagttttct tgttagtgaa tgagatactc      300
ctatgagtcc ttggatagta atactggtca aggcaccata gacagcatag gcaaatgtat      360
atagtagtcc ccccttatgc atgattttac tttctgtggt ttcaattacc tatggtcaac      420
cttggtccaa aaatgttaaa tggaaaattc cagaaataaa taattcataa gttttgtttt      480
ggttttgaga cagggtcttg ctccagccca ggctggagtg cactggtgta gtcatagctc      540
actgtagcct ccaactcctg ggcttaagca gtcaagcctc agcctcccaa atagaactac      600
aggcatgtgc caccatacct ggctagtctt ggctatttttt atttttattt ttatagggat      660
gcagtcttgc tatgttgccc aggctggtct tgaattcctg gcctcaaata atcctcccac      720
ctggcctccc aaagtgctgg gattataggc aaaaactact gcacctggcc ctaattcata      780
ggttttaaat ggtgcactgt tttgagtagc acaatgaaac cttgagctgt cccattccat      840
ctggcctggg atgtgaatca ttcttcgttt agtggctcca cactgtatat gctacccgcc      900
cattagtcac ttaatagcca tcttgcttat cagaccaact gtgagagtat tgctgtgttt      960
atgttaagta acccttatat tacttaatga ttatccaaag cacgacagta gtgatgctgg     1020
caattcagat gtgccaaaga gaaactgtaa agtgcctcct ttaagtgaaa aggtaaaagc     1080
```

tctcaacaaa aaaaaaaaaa aaaaactcgt ag 1112

<210> 142
<211> 1084
<212> DNA
<213> Homo sapiens

<400> 142
ggtttggggg catcacagac tacacccgta tgagaggatg aacttaaatg ataaattgtg 60
tgtgtgtgca tgcatgtgtg cgtgcatgtg gactgttaca ctcattggtc cttctgctgt 120
ctctctccct ctcctcagcc ctctttattc cctgggacac agaaattttt aaataaggcc 180
aattaataat cctacattgg tctcttacgt gttagagtga aaagaagatt cacatatctc 240
tcatttaaaa ttgaaagcta gaaatgatta agcttagtga ggaagccatg ttgaaagctg 300
agatagtcca aaaactaggc ctcttgcacc agttagccaa gttgtgaatg caaaagaaaa 360
gtgcctggag gatatttaaa atgctgctcc agtgaacaca caaacgatag gaaagcaaaa 420
tagccttatt gctgatatgg agaaagtttt aatggtctgg atagaagatc aaaccaactg 480
caacatttcc ttaagcaaaa tcctaattca gaacacagcc atagctgtct ccaattctat 540
gaagacagag cagagaggaa gctgtggaag taaagtttga aaataagagg ttgttcatga 600
ggtataagga aagaagacat ctccataaca taaaagtgta agtgaaacat caagtgcgaa 660
tacagaagct gcagcaagtt atccagaaaa tctaagatca ttgaagaagg tggctacact 720
aaacaataga ttttcaatat agacaaaaga gccttctgtt gattttaggc atctagccta 780
aaatggaaga agatgccatc taggacttta atgggtagag aggagaagtt gatacctgtc 840
ttcaaagtaa agactgactc ttttgttagg ggctgttgca gctggtgaca ttaagttgaa 900
gccaatgctc attcaccatt ccagaaatcc ttgtgccctt aagaattatg ctaaatctac 960
tctgactgtg ttctacaagt agaacaacaa agcctggatg acagcatatc tgtttatagt 1020
catggtttac taaatatttt aagcccactg ttgagaccta ctgctcagaa aaaaaaactc 1080
gtag 1084

<210> 143
<211> 1050
<212> DNA
<213> Homo sapiens

<400> 143
ggcacgagct tttcagcatt tgatggttgc tgaccactcc cactttcaca gaaccctcat 60
caaacagcct tctatgatcc caaatgcaac tttctatcac atttttatgc tcttcttctg 120
cctactcatg aaaatgttgg ggccatccag gcttccattt ttagccctca ctttgtgcag 180
gtttatactt tattttcagt tttgttatct gatctctgac tccagcccag accattcctg 240
actccacatc cacatattca tctggcttgc tgaataactt ctcttggatg tacatgtgtg 300
ccttagactc attatgtgca gacatgaagt catcttttt ctctccagac ctgcttttcc 360
tctcgtattc ttctttttgg tgaatggtac aattattcag atggaacgtc caagtcaaaa 420
gtcgttctag aatcctccct cactcctaat gccacatcca attagtgacc aaatcctatc 480
gattcggcct tctaaataca gtcaaaacat ttcattcaat tcagcgtcac tgtcattgct 540
ttaatgtaga ccttctctat tttaccatga tcaagcagag gccctgtatc tatattcttc 600
tgccttccag tcttgtcatc ctactccgca gttaatcccc tgagtgctat cctagtgatc 660
cttctaacag tacagatttg gtcatggatt ctccagcttg aaatacttca tgtctttttgt 720
gggaacatgg atggagatgg aggctattat acttagcaaa caaatgcatg aacgaaaacc 780
aaataccaca tgttcttact tataagtggg agctaaatgc tgacaactca tgaacacaaa 840
caaatgaaca gcaaacactg gggtctactt gagggtggag tttgggagga gggagagaag 900
cagaaaaggt aactattggg tactgaactt aatacctggg tgattaaata atctgttcaa 960
caggccccca tgatatgagt ttacctacgt aacaaacctt cacatgtatc cccaaaccta 1020
aaataaaagt taaaaaaaaa aaaaaaaaaa 1050

<210> 144
<211> 1113

<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (349)
<223> n equals a,t,g, or c

<400> 144
gttggtgttg agcacagctt taggcttaga ttcttcatca actaggagaa gctgtgcttc 60
aatacagtta ttcgtttgca tggttcctaa tgtgcttcac tcaatttagc agaatttttt 120
ttttaacctc ttccttgacg ctagctgctt gtgcaaatca catcttggcc gcctactctt 180
cttcacttgc tgacagatgt gtaggtgaga aaagtctcat agtcattgtt cctgaaagaa 240
gcttccagac ccacttctag ggccagtgac atatgcagga aatcagctgc ttctgggcca 300
ggacagagct ggtctttttt ttagtggggg atggcgggca gtggggcang ggacattcaa 360
aatttatttt ccaacagaca gatagcatca gcaggtacaa ctacaagggt atctacatag 420
atcatacatt cacaaggcat tattagttca acagtgagaa agccactcgt gggttttctg 480
taacaatatc ccacttcata gtgtaaacag gtactatttt gttcacttac aattccggaa 540
ggaagggcac accttgcagg ggggaagaaa aggggaatcc taaagtaagg tgcaacaatt 600
aagagacaac actttggcta acaatcttgg atccacattt cagtcagggc cttccacata 660
gaggggaaag actttttctct cagaagttag aatctttctt cctcctttct tgttaaactg 720
agagcagtgt tttgtttgct caatattaca tgtacaaaag gagattagaa gaaaatgcat 780
cacaaaacca tcttgaacgt tcagctcttc ctgccaatac atcacaactc ttaggtttta 840
gacggggcct gggaatacgt aagtgttttt tctttttttt ttttttaagt gaaagcaagt 900
ttattacgaa agcaaaggga taaaagaatg gctgctccat aggcagagag cagcccagta 960
atcttaaaat aggaaaatag acactatggc tacaaaaaat aaaaaataaa tgaggtagat 1020
aaaattttca cacccaggac ttgcctgttc caacttcata gtcttcatga aatattcatc 1080
aagaagacaa aaaaaaaaaa aaaaaacctc gta 1113

<210> 145
<211> 685
<212> DNA
<213> Homo sapiens

<400> 145
ggcacgagca cttcctgaaa taaaagggag ccgcttacaa gaaataaatg atgtatgtgc 60
aatctgctat catgagttta caacatctgc tcgtattaca ccgtgtaatc attatttcca 120
tgcactttgc cttcggaaat ggctgtacat tcaagatact tgtccaatgt gccatcagaa 180
agtatacatc gaagatgata tcaaggataa ttcaaatgta tctaacaaca atggatttat 240
tccacccaat gaaactccag aggaagctgt aagagaagct gctgctgaat ctgacaggga 300
attgaacgaa gatgacagta cagattgtga tgatgatgtt caaagagaaa gaaatggagt 360
gattcagcac acaggcgcag cagctggaag aatttaatga tgatactgac tgatgaaaat 420
agcatttatt aatgattgag gtatttgttt aaaattcagt tcatccaaaa tggagtaata 480
tccttcacct tcagtgtgta accaagcaca aaaacagtat caatgttgaa tctgtgaatg 540
gttttccgtt tactgtgatg tgctactgta aatatacctc tttaattact tctggtctct 600
ttggtgacct gtttaaattt gtgtacatta ttgtacatag aataaaatgt tttcacattt 660
ttatgacaaa aaaaaaaaaa aaaaa 685

<210> 146
<211> 1038
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (743)

<223> n equals a,t,g, or c

<400> 146
ggcacagtga agccatctat tgacaaatgg aggagaatga tgaaaagttg taagatgttt 60
aaatattttg ctattattca tgattattcc taaattttat cttttcaaac tgttgctact 120
acttcagaag attacacatt ttatctgtgg caagacactg aacaatttaa attttaggtg 180
tgaatcatat ttcctgtttc tgtacctcta ttgtgcatac atattatact aattcttaac 240
aggaaaaaat actttttck tttttatctt tgtacttttt tttgaaggtt ttaatttgtt 300
ttagagatgg aataaaaaag ctgtgatgat atataatcct aataataaaa ttacttgatc 360
aacggttttg aaaaataccc ttwaaaaata atagggcatg gtggctcata cctgtaatct 420
cgtactttgg gagggcgaag tgggcggatc acctgaggct ggtcttgaac ttctgrgctc 480
agacaatctg tccacctcgg cctcccaaag tgctgggatt acaggcatga gcccactgca 540
cctggctgtt atgtcctttt gatgaatcaa ctctttcata attataaatg actcttttta 600
tccctggtaa tgtccttttgt atagaaatct ttttttttt tttaaataag aaacagagtt 660
ttgctctgtc aggctggagt gcagtggtgc agttataact aactgcagtc ttgaactctt 720
ggccacaagt gatcctcctg ccnyggctca tacctgtaat cccagcactt tgggaggccg 780
aggtgcgcgg attgtctgaa gtcaggagtt tgagaccagc ctggccaaca tggtgaaacc 840
ccatctctac taataatata aaaattagct gggcatggtg gtgggcacct gtaatcccag 900
ctactcagga ggctgaggca ggagaattgc tcgaacccgg gaggcggagg ttgcagtgag 960
ccgagatcac accactgcac tccagcctag gtgacagagt gagactctgt ctccaaaaaa 1020
aaaaaaaaaa aaactcga 1038

<210> 147
<211> 851
<212> DNA
<213> Homo sapiens

<400> 147
ggcacgagaa caaattgata gtgagcatta agggtttcca agttggattt gtaactcctc 60
atcattcctt gtatgacaac tttctgaata tatgtcacta tgtagtaaaa ttaaacactc 120
caaactcatc tttctgttgt tagaagtttt cagcggtact tccatgcaac tttaaatctc 180
actgctctct atggttgatg tcaaatgacc ttcagtaatg actgagaatt gaatacaaat 240
agattacaaa gccaaaattt gatgttaaat gactcaggaa attttagttg tattttcaat 300
tcaagtactt agtagcctac gtttgcttgg cctctggttc tttatggaaa ataggctttg 360
tagtggcatt gtggagcaaa ggagactgtt acaccttaat taacttttt tactgatgca 420
aataatttga ggatagagag gagggaagta gtgaaagcta tgacctaaaa cattgggacc 480
aaatagaggc tcacagatat ttggattatt ttatgtgctt attattaaat aaggaaagca 540
ttttgtgata tgtggaagac gctatgtgaa gttttaccta tcttctcaaa gacctttct 600
tttgtatttt cttttggtgt ttcttaaagc caaacaaaga aatgttctta aggagacagg 660
gtgggttttt ctgtgggcct ttgttggttt ttctgtkggc catcgccctc taatggaatt 720
gatctctggc tgtttgattt ttttcatatt gtatttttaa aatttgttgt acagtgccct 780
gtgagcacca agtaccacta gatgaataaa acgtattata tctaaaaaaa aaaaaaaaaa 840
aaaaactcga g 851

<210> 148
<211> 614
<212> DNA
<213> Homo sapiens

<400> 148
ggcacgagcc aatatccact ctacccagct gggcccccag tctacaaccc tgcagctcct 60
cctccctata tgccaccaca gccctcttac ccgggagcct gaggaaccag ccatgtctct 120
gctgcccctt cagtgatgcc aaccttggga gatgccctca tcctgtacct gcatctggtc 180
ctgggggtgg caggagtcct ccagccacca ggccccagac caagccaagc cctgggccct 240
actgggggaca gagccccagg gaagtggaac aggagctgaa ctagaactat gaggggttgg 300
ggggagggct tggaattatg ggctattttt actgggggca agggagggag atgacagcct 360

gggtcacagt gcctgttttc aaatagtccc tctgctccca agatcccagc caggaaaggc 420
tggggcccta atgtttgtcc cctctgggct ggggtggggg gagggaggag gttccgtcag 480
gcagctggca gtagccctcc tctctggctg ccccattggc cacatctctg gcctgctaga 540
ttaaagctgt aaagacataa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 600
aaaaaaaaaa aaaa 614

<210> 149
<211> 1200
<212> DNA
<213> Homo sapiens

<400> 149
ggcacgagga gagagaagat gatgaaaaga ctgttgatga ccgaactgtg aaattctccc 60
cttgtcacct ggaagatggc atggtgcctt ctgtccgtct tctttcttcg ggctttgtgt 120
gctcactcta gcacagcata caagtgtgtg ctttgttcgc ccaggtctcc atggttagtt 180
gaagccaatt tctggcttga cttttatggg aaaagttatt ttatgtctcc taagcattag 240
agtttttcta ttactctatg tagttgagac aggatttgat aagtctagga aaagaaagat 300
gggaaaacgg gattcctttt cagaagtacc tgtgtgtatc tgttaataac cacaggggtt 360
aatatgatgt aggatctttt actatcaatt tcaaccattt gattttgtat gattgaaact 420
tgcaccgagc tttgactgtt tgttaaagag tcatttttaa tgaaagaata attctttatt 480
gctggttttt catttacact gataaataca cagatcttaa taaagtcttt aacattcatt 540
tgtattcaga tgtgagtaga agaactaaaa aaagaaagtt acatatcact atgactgaag 600
gtacttcagc ttaatctgaa atataattta acttgtgaac tccttggata tgatattatt 660
tggaataaac agaatttatc attgaaccca aagtaggaaa tgatagctta cattgtctaa 720
aaatccttac aaggttaaga tgattcaata tcaagaatat tcagaaaatt atttctaaag 780
ttgatcgatt catgtcgtat tgatagaatc ttgaccagaa gaaattttgc tctttttata 840
tagtttcaag aaatgtgttt ttaaattttt attaatgcac ttgaacaact ttgcaggaat 900
aaagcaaccc cctaaccaca aaatatccct ctaaattagt tccctagctt tctcaatgaa 960
tacacacata tttttacata gctatgatcg ttgtgtacat tctccttttgt tttacttctc 1020
ggcctaacac ttgtctcctc ttgtcaacac agattctact ctcaccaatt taaatgtctt 1080
tatatccatg ttacatgggt aacctcactt caccccatta ttagatattt gagttatatc 1140
taatttttca ctcttataaa tagtgctgct atgaatgtct gtaaaaaaaa aaaaaaaaaa 1200

<210> 150
<211> 683
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (41)
<223> n equals a,t,g, or c

<400> 150
gggagaatag gttagaagaa aatatctacc ctgagacagg naaaaacaag aaaatgacat 60
atacagaaaa gagcatatga gacacaggaa ctggtagtaa agtctatgaa aggctgttgt 120
ctctcaccta gtgttgggcc taaagttgct gcagtcagaa aggcctgcag ttaaaaggaa 180
aagttggatg tcaagtggga aatactgaga agaaaagttc tcagaggaag caatatcctc 240
cctaaaaacc aggaactttc gaacaactca agggtccact ttcaggtcaa gtgctgaaag 300
gcaatgcaga tgacagttgt atggtatgtg attactgcaa tcatttggtg gagaatgagc 360
atgtgtgaag ccctctcaca gaattgcttc taatcctaaa atgtatctca ctgtgatgaa 420
aaacaatcaa agtacagttt agactaaggg atgtgtcctc aagtttagca gactcttaaa 480
cacttacttc tagttgtagc ttgattattt cattttgttt ttcttttttct tgacttctta 540
gctttgcatt taactctgaa atttccatct ccttttttctc tattagttct ttgtgctttt 600
cttcatttaa ttcaactgaa taaaatgaaa taaataaaat tcatttgtta aaaatttcaa 660
aaaaaaaaaa aaaaaactcg tag 683

<210> 151
<211> 827
<212> DNA
<213> Homo sapiens

<400> 151
gggcacgagc ttgggcctca agtgattctc ctgccctcag cctctcagga caaccccagt 60
tctgtcatcc acgtggtgaa tcagaccaat gcccaaggcc agcaagagat tgtytamtat 120
gtgctgtctg aagcggcacg agcctccccc agcccctgag ccaccttcag ggggcatcat 180
ggaaaagctt caaggaatag ctgaggagcc agagatccag atggtttgaa ggccgcagag 240
ccagaccatt tcttccccag gtcctgaagt ttgagccagg caagtggcag tgcccctagt 300
gggcagccgt tgccaatgga tgcctttagg agtggtgccg agagcagtgt ggtccactct 360
ggcctgggtt tgcatcattc tgcagactct aaagacttcc cttttctgcc agactacatt 420
ttgtggggag cctgaggact ctggattctt tgaggggatc ctggatgtgt gtgttcttgt 480
taaagaggct gttatcaggc ttaaccataa ccctcaagat ctgcttgaca gtgattaaat 540
ccttagctca catccattcc catctttcgg gctccttagg cccaaggatg gcatgtgact 600
ggtccctgca agggtccttt ctttgtcacc agccaaggca ttgataacca agtagccatt 660
ttcctcttaa ggtttcctct acaaccccaa ggactttcat gattatcctc agggacagga 720
ttggaggcat tgagcgtgtt tattaacaaa ttgtttttgg taataaaata aatgcttgga 780
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaa 827

<210> 152
<211> 835
<212> DNA
<213> Homo sapiens

<400> 152
aaaatatttt ggtagtaatt taaaatacaa gaacgaatat ttatttgtcc acagttggag 60
atgttggata aatgtctttt ctcaaagatc acaggacttt tgtctttcat ttttgccttt 120
ttatttacca tttataaaag atctggtctg gattatggaa tttaatgttt atcagctcta 180
tgtattcctt tatagaggct tgaggaagta tttcacataa catgttttat aatacttaac 240
catttatcca aagatatatt tacattgggt tgtgcccctt tcccttagat catggtaaat 300
ttttcttatt gaggtaatta tgtactactt atatttgaag gaagcttatg acattttaca 360
gtagctaaaa tgttgagatt agaggtactt ttactattct tctcaaaggt aactgatcag 420
ataattaccc aaattattca agaaaataga tcagaaataa agaacaacat aattttctaa 480
gaattcattg aaatttatgg aatcagctct cgcactgccc atctttgcag ttttgaaaaa 540
gaaattgctt aatcacaaat gttctacagt ctttaaatgt agtagaatta gacagtgaga 600
tcatctgagt aaattgattg gtgattccag agataagact aatattttaa attatttatg 660
atactgatta gtataaaaac gtactcatca cagaatttga agcaaaatac atgtacactt 720
caaagagtaa atgacaaatg tataaatgct gtagctcagg attatatgta cctttaaaaa 780
tacactaata aagattattg ttcaaaaatt aaaaaaaaaa aaaaagggcg gccgc 835

<210> 153
<211> 558
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (27)
<223> n equals a,t,g, or c

<220>
<221> SITE

<222> (39)
<223> n equals a,t,g, or c

<400> 153
cgggaccgga taacaaattt caccccngga aacaggctnt gccccactag gcttttggca 60
aaaaagctat tttaggttgc cactttagga ggtacgcctg gcaggtaccg ggtccggaaa 120
ttcgcggccg cgtccgactc atgactgtgt tggcacttta aaaatattga tatcccacaa 180
taaacagggt tatcattgat ataatttccc acatatttta ctataaataa tcgagtaaca 240
acctgtcttg taccattctt tacagaaagg cttttctcaa tgcgttagtc agggtttctt 300
cccggggaga aaatttataa tccttaatga ggccagtact cagaaggaca tttctgctta 360
ctcttttctc tgtaattgcc ctcactaaaa taaagcatga ctttttttatc atgtgttcac 420
acatgcagtg catccctaga gtttttctga agcatgaatt caataacata taattagacc 480
tgattctgag aagattttct cttcttcgtc gacgcggccg cgaatcccgg gtcgacgagc 540
tcactagtcg gcggccgc 558

<210> 154
<211> 1201
<212> DNA
<213> Homo sapiens

<400> 154
ggacatttgt aaccctataa acactagtaa attaaaaaca gaaggacctt tatgtcctaa 60
catatctgtg ttgtgaaagg ctgccctgtg aaatacggga tttcttaaac atattttaaa 120
aatcataggt gtcaatattt tttagaaatc catttaaatt ttctcttgtt attttacaat 180
gcctatttat ttatatagtg gctctgctga ttttgatgta tatcctaaag tttatatttt 240
ctttaaagga tgttttatac aactttatgt aaaatgtttc agtatcttca cattctctcc 300
ctgtcctttt gttttgctct tatatggtgg tctgagtctt ttctctggct ttcaaaccta 360
gtaagactaa gacactaaag taactttgcc cgaggtttgg gtaatgcctk cyaaakcaca 420
tcctaagctc tcgtgcatac aggggcctcc tttgagctct gtgcttttga gatcccatac 480
acctaaattc cagtactcca aatcagtact gctcagtttt agtgactaag tttaaaaatg 540
tattttaata rcaagttagt ttagtgccct cttgcttctt tctcgactgc ttgtatacat 600
gtatattcct ttaaatgaat cttggaattt atttagaaat attaaattat actaatgaaa 660
ctgtatattg ttgkgaattc ataagtgaat ttggaaagaa tttgtcttta tgaaactaaa 720
tccttttttat tcaagaatca tatgtgtctt tatatttatt ccagtctaca tttatatcac 780
tgagtaaata tatagaaatg tggatacata cagctgtagt tacagataca aatatagata 840
taacctgtta aatctatatc tatcccatat aacatatata catgtaatat gtgtgtgttt 900
atatatatat gtttatgtca ttaaagagct cccttaatat ttttctttta tttcccttat 960
aatttgaggt tgagcttgaa ttttccttgt ataaacaagc aaatatttat actagtttta 1020
atactgatgt ttagacattg tatcttattt tagcgctgaa tattttcaca attattataa 1080
atattatcta atactaataa tgtacctgtt aaaaatattt aaaattttac ctttgaatta 1140
ttttattgtt gaattaaaat tcctttaata tgataaaaaa aaaaaaaaaa aaaaactcgt 1200
a 1201

<210> 155
<211> 1026
<212> DNA
<213> Homo sapiens

<400> 155
gtctaaatgt tcagtttttc ttcctaattc caatgattct cctcatttct caatgtcctt 60
tgtccatctt tgctgctcca tttgcactgc ctcccaaagg tcactgtggc tcctttctctg 120
acttccacag tcaagttaca cttcataaaa attctaagct cattttcaga agccacaaat 180
ctatccttct ttaaagtctt caaactttga ttgtgtaaat aaatactcag aaacaagatt 240
tctaaaaaac aaacactatt ggccatcgta tgttcaaagg agataacaaa tgtttaacct 300
tatatgttgt aggctttcta aacttaattt caaaaaaaga ctaaataaac agtgtcaata 360
tgtctataaa ctcacaacga aaattttcag atcatccaat tgtgtattca ttggccggaa 420

acaatcatgt aaaaaccaca gccctggagc tgggtagcat agaaacaaga agattcagca 480
tttcatggtt ggtgactcaa atctctaaag ggktgtcagg ttaaaaaaaa aaaargaaaa 540
gaaaagaata gaaatttgac ctgatctata aaaatgaaag tcgctgggca aagttttggc 600
ttttcactcc tgacaaagat gagctctctc ataggtagac caaggcacac gagtgatgac 660
tttcgtggcc ccaaaatttct tcaagaaaat agtagattga ggaagcgatc tgcgcattga 720
tagaggtgct gtttgaactg gatgacattt aagcttcctt ctttctccaa gattctgtga 780
ggccatgaag catgctattt catccccact ccaattgctg tctcccctggc ctggtgccct 840
taccacctca atcttgggtc actgatctct tttgcaagaa atcagtcctg cctaccacct 900
gcaacttcat cttcctaaaa tgtcactttc cttaaggcct gctctgttca aaggccagtt 960
cccagccaca ccaatgtaaa ctcgtgccga attcgatatc aagcttatcg ataccgtcga 1020
cctcga 1026

<210> 156
<211> 904
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (8)
<223> n equals a,t,g, or c

<400> 156
acccacgngt ccggagtata cttaatttta tttatgtata gaatatttgt atttattttt 60
tggacatata tttatcactt tgtcattttt tttaaccaat ttgagaaatg ttagctgctg 120
aattaatttg ttgcccgagc cttcatattt tcttctttgc tgccttctcc ctgtggcaat 180
gtactgttct cacaatgcct tttaaaaatg ttccatactg tattagcatc cttagaaggg 240
acagaactaa gaaatacatt gctcaaataa tattttactt tattgataat gacaaagaat 300
atttttaaa ccccatcaaa atagatttca attgactgtt tcccctacat cttttgagcc 360
acagtcgccc atcgaataag caaatttgtt tttgagaata aactggtaac cagtttgtga 420
tgactctcag aagccttttg gctgggatac agaagagttt ctaagttcct agagagccat 480
ttaataatta gttggtgagc cagaggcttg acagagctgt tacttatgtg tgagggcttt 540
attctcaggc agtagtttat tcatcatttg gtaagcccct ccccacactc ctctaattta 600
aacaagtagt gaaggcttat cttaaactgt gtagtacctt agacttggca tttatttttg 660
atagagcaga gataaaatat tttgatggaa ggaaatcaat tttctgtaac tgatgatgtg 720
aaaatttat tttctgggaa attatatagc cattcaaaaa ttcaaagtat gttattatga 780
ttggttacaa gagaataatg ttacatgttt aattgtaata tttgtctcct atcattttct 840
tccctttcag tcataataaa tgatttacaa aacccaaaaa aaaaaaaaaa aaaaagggc 900
ggcc 904

<210> 157
<211> 916
<212> DNA
<213> Homo sapiens

<400> 157
gtttgtgtaa ccatgttctt cagaatgcag gtatgtgagc atcatggttt ctgggtaatt 60
ctgctgctcc tgtctttgaa aatggagata ccacttgcag cttatcccac tgctgagtat 120
tccagcattg gtagtggttt cactccattg catccatcca gaactttcac acaggcctcc 180
ccattaccca gcatttttta acattgatca ataaggccta taaccagatt taggctagca 240
acaccagagg tctgggggca agggtggaaa ttgactttac attcttagta gctaatattc 300
cataagtgct ttatatatat attgttgtta ttgatcatct attcaaaaaa tatatattga 360
gcagctgctg tggtataggc tctgtgctgg ccagtgaaga tacatgatta acaatgttgt 420
gcttgcttgg ttcacagtcc tgtgggtaca tggtggagta aaataagtac aattaatttc 480
tcagagctgt gcacagcaac acacagaagg agagataact cacccagctt cagaggggtg 540
ggacagagaa tgaggttagc ctcccagatg tccttgtgct agttttagct gttttcaggt 600

gttgataaaa gctccaggag ctggcaggag gagagcagag gaagctagag cttacaaagc 660
acaaaggcca tgacagcatg ccagacgggt gaaagaggac aggggaaatg taggcaagtg 720
tctcttctca gaggatgtta tatactatgt ttaaaagtgt tgatctgctg ggcacagtgg 780
ttcacgcatg tagtgtcagc actttggggt gccaaggtgg gaggattgct tgagctcagg 840
agtttgagac cagcctgggc aacatagtga gaccccatct cttaaaaaaa aaaaaaaaaa 900
aaaaaagggc ggccgc 916

<210> 158
<211> 921
<212> DNA
<213> Homo sapiens

<400> 158
ggaactgctg ctcatggaac tggctcctct cctcttgcca cttgagtctg ttcgagaagt 60
ccagggaaga acttgaagag caaaatacac tcttgagttt gttgggtttt gggagaggtg 120
acagtagaga agggggttgt gtttaaaata aacacagtgg cttgagcagg ggcagaggtt 180
gtgatgctat ttctgttgac tcctagcagc catcaccagc atgaatgtgt tcgtagggcc 240
tttgagtgtg gcgattgtca tattctgttg gataacaatg tattgggtgt cgattgtcat 300
ggggcagggg agagggcagt acacctggag gaccattttg tccacatcga caccatcagt 360
ctgctcttag aggatgccct ggagtattcg gcgttgattg cggggcaccc gaaatcagac 420
ttgccacctg gactgtcgag gtgcagaccc tgggagcacc actggcccat ctcttacaca 480
ggctgaccga tttctcctgg tgttcagagt ctgtttttgt ctagcaccat ttgaaatcgg 540
ttatgatgta gggggaaaag cagcagcctc gaagcctcat gccaactctg ggcagcagca 600
gcctgtggtt tcctggaaga tggatgggca gagaataggg aaggaagatc atgcttttcc 660
ctactaactt ctgtaactgc atgtatgata cattattgca gaggtaagag atagtttaat 720
ggatttttaa aaacaaatta ctataattta tctgatgttc tctagttgca ttttgctgaa 780
atgtagtgct gttctaaatt ctgtaaattg attgctgttg aattatcttt ctgttgagaa 840
gagtctattc atgcatcctg accttaataa atactatgtt cagttaaaaa aaaaaaaaaa 900
aaaaaaaaaa agggcggccg c 921

<210> 159
<211> 804
<212> DNA
<213> Homo sapiens

<220>
<221> SITE
<222> (800)
<223> n equals a,t,g, or c

<220>
<221> SITE
<222> (801)
<223> n equals a,t,g, or c

<400> 159
aagaaaactc tagaagtctg gatgtcggtg ggcctctgag atatgccgtt tacggttctt 60
cttcacaggg ccgctgagtc acttcttcta cttcttcatg gaacattgga tccctcctga 120
ggtccccctg gcagggctca ggaggcttct cctggaccgc ctcgtctttg caccggcctt 180
cctcatgttg ttcttcctca tcatgaactt tctggagggg aaagacgcct cagccttcgc 240
cgccaagatg agggggggct tctggccggc gctgaggatg aactggcggg tgtggacgcc 300
actacagttc atcaacatca actacgtccc tctgaagttc cgggtgctct tcgccaacct 360
ggcagctctg ttctggtatg cctacctggc ctccttgggg aagtgacgac cgctgggaga 420
acatcaggtg cactgtggac gtgggtctgg gggtctcacc cgcccagcga gagcagaacc 480
aatccagtca ggatgtcact gactctaaat caggtgattc aagatgccca aaaatgatgg 540
atagagaaac agaaatctct gaatgtcaga accctgtctt ttaaaaaggc agtcrctgcc 600

```
ttcaggtggt gctgccccag aaacttaaaa tttagtcgag gcagtttcaa ttgttactgt      660
ggaccgaatt aggatcacaa taaacgataa tgcaggttct tcaaaaaaaa aaaaaaaaaa      720
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaactc gagggggggc ccgtacccaa      780
tcgccctgat gatgatctgn ncac                                             804
```

<210> 160
<211> 24
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (24)
<223> Xaa equals stop translation

<400> 160
Met Tyr Gly Cys Val Cys Val Cys Ile Tyr Leu Tyr Thr Cys Ile His
1 5 10 15

Gly Cys Pro Cys Val Ser Met Xaa
20

<210> 161
<211> 113
<212> PRT
<213> Homo sapiens

<400> 161
Met Gly Ser Trp Cys Ile Cys Thr Leu Leu Leu Leu Leu Thr Asp Gly
1 5 10 15

Gln Gln Gly Phe Tyr Pro Gln Pro Phe Gln Ala Ala Pro Gly Arg Gln
20 25 30

Gln Leu Trp Gly Gly Thr Asn Pro Trp Ala Val Leu Ile Pro Glu Ser
35 40 45

Phe Leu Pro Tyr Thr Leu Thr Val Asn Tyr Ser Pro Ser Cys Asn Phe
50 55 60

Glu Phe Tyr Leu Pro Lys Met Arg Leu Ala Tyr Ile Cys Met Ser His
65 70 75 80

Ser His Cys Pro Tyr Leu Gly Arg Asp Ile Ile Ile Thr Leu Leu Asn
85 90 95

Tyr Cys Ser Ser Phe Leu Ala Glu Leu Leu Ala His Leu Val Tyr Ile
100 105 110

Ala

<210> 162
<211> 45
<212> PRT

<213> Homo sapiens

<220>
<221> SITE
<222> (45)
<223> Xaa equals stop translation

<400> 162
Met Thr Lys Arg Arg Lys Pro Arg Tyr Arg Phe Ile Phe Ala Leu Tyr
1 5 10 15

Ala Leu Arg Leu Val Phe Leu Phe Arg Ala Val Thr Asn Thr Asp Ala
20 25 30

Ser Arg Leu Arg Ala Lys Arg Gly Glu Cys Pro Tyr Xaa
35 40 45

<210> 163
<211> 59
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (59)
<223> Xaa equals stop translation

<400> 163
Met Thr Glu Gly Leu Leu Ser Ser Leu Ser Leu Leu Leu Tyr Leu Leu
1 5 10 15

Thr Trp Leu Leu Met Leu Ser Lys Lys Leu Tyr Val Gln Met Ile Phe
20 25 30

Cys Tyr Asn Pro His Phe Ser Gln Met Asp Ala Cys Asn Gly Thr Ser
35 40 45

Gln Lys Ile His Asn Ala Arg Gln Cys Thr Xaa
50 55

<210> 164
<211> 118
<212> PRT
<213> Homo sapiens

<400> 164
Met Cys Tyr Leu Leu Leu Leu Leu Ile Gln Thr Ala Glu Leu Leu Ile
1 5 10 15

His Pro Gln Gly Leu Gln Ala Val Ser Asn Gly Glu Ser Ala Leu Lys
20 25 30

Gly Thr Arg Pro Thr Phe Ser Ser Pro Phe Ile Leu Val Thr Glu Gly
35 40 45

Arg Lys Glu Trp Glu Gly Val Phe Leu Ser Ser Gly Trp Lys Gly Asn

```
    50                  55                  60

Thr Leu Ser Asn Tyr Tyr Ile Ser Leu Val Phe Tyr Tyr Ser Arg Ile
 65                  70                  75                  80

Leu Gln Pro Tyr Phe Tyr Cys Leu Trp Gly Lys Leu Glu Met Val Thr
                85                  90                  95

Leu Ile Arg Ser Val Trp Arg Gly Ile Asn Gly Gly Asp Lys Ile Ser
            100                 105                 110

Val Gly Phe Gly Lys Cys
        115
```

<210> 165
<211> 55
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (55)
<223> Xaa equals stop translation

<400> 165
```
Met Cys Ser Gly Leu Leu Ser Met Thr Phe Ser Phe Leu Leu Glu Phe
  1               5                  10                  15

Cys Ser Val Ala Gln Arg Leu Arg Leu Ala Asp Ala Arg Thr Ser Met
            20                  25                  30

Gln Asp Ile Leu Lys Trp Phe Ser Asp Tyr Thr Leu Arg Ala Asp Ile
        35                  40                  45

Ser Lys Ser Arg Asp Leu Xaa
     50                  55
```

<210> 166
<211> 127
<212> PRT
<213> Homo sapiens

<400> 166
```
Met Gln Gly Ser Asp Ala Gly His Gly Gly Thr His Ile Tyr Arg Ala
  1               5                  10                  15

Leu Val Gln Trp Pro Leu Ala Trp Val Phe Tyr Leu Ser His Ala Lys
            20                  25                  30

Thr His Trp Gly Glu Glu Leu Arg Phe Ser Phe Arg Arg Lys Asn Leu
        35                  40                  45

Arg Leu Arg Glu Ala Met Arg His Glu Thr Cys Gln Val Thr Gln Leu
     50                  55                  60

Val Ala Gly Lys Ala Asp Ser Asn Leu Cys Leu Arg Asp Ser Glu Thr
```



```
 65                  70                  75                  80

Trp Phe Trp Pro Pro Leu Trp Ala Ala Cys Ser Ser Leu Gln Ala Thr
                85                  90                  95

Ala Cys Arg Leu Ser Ser Pro Ser Lys Gly Leu Gly Ala Ser Arg Glu
            100                 105                 110

Cys Pro Trp Leu Ala Ser Gly Arg Ala Ala Leu Val Ser Phe Leu
        115                 120                 125
```

<210> 167
<211> 56
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (32)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 167
```
Met Gly Val Glu Gln Tyr Ser Tyr Leu Phe Leu Thr Cys Val Phe Met
  1               5                  10                  15

Cys Val Ser Leu Gln Trp Lys Ser Thr Gln Pro Trp Val Gly Asp Xaa
            20                  25                  30

Thr Cys Met Arg Lys Gly Ile Thr Gly Thr Glu Val His Arg Thr Asn
        35                  40                  45

Ala Leu Phe Thr Phe Trp Cys Ser
     50                  55
```

<210> 168
<211> 73
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (73)
<223> Xaa equals stop translation

<400> 168
```
Met Pro Ser Ile Arg Leu Gly Leu Ser His Leu Phe Leu Thr Ala Gly
  1               5                  10                  15

Ile Tyr Cys Leu Leu Leu Cys Ala Arg Cys Cys Ala Leu Gly Arg Gly
            20                  25                  30

Thr Ala Trp Ala Ala Cys Pro Gly Gly Ala Cys Gly Leu Met Gly Glu
        35                  40                  45

Ala Asp Pro Ser Pro Pro His Cys Gln Gln Gly Gln Gly Lys Ser Thr
     50                  55                  60
```

```
His Arg Gly Leu Ile Pro Tyr Val Xaa
 65                  70

<210> 169
<211> 70
<212> PRT
<213> Homo sapiens

<400> 169
Met Thr Pro Gln Asn Leu Arg Phe Thr Leu Phe Gln Phe Cys Tyr Ser
  1               5                  10                  15

Leu Tyr Leu Glu Leu Glu Leu Gly Phe Arg Ser Leu Ser Gln Glu Val
             20                  25                  30

Thr Arg Glu Trp Cys Leu Ser Tyr Phe Phe Leu Ile Lys Val Cys Trp
         35                  40                  45

Gln Val Pro Val Ser Glu Phe Leu Leu Val Lys Glu Asn Pro Phe Leu
     50                  55                  60

Leu Leu Glu Lys Lys Leu
 65                  70

<210> 170
<211> 80
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (80)
<223> Xaa equals stop translation

<400> 170
Met Pro Phe Ile Leu Leu Leu Val Cys Leu Thr Ser Leu Pro Ser Arg
  1               5                  10                  15

Gly Tyr Asn Glu Lys Lys Leu Thr Asp Asn Ile Gln Cys Glu Ile Phe
             20                  25                  30

Gln Val Leu Tyr Glu Glu Ala Thr Ala Ser Tyr Lys Glu Glu Ile Val
         35                  40                  45

His Gln Leu Pro Ser Asn Lys Pro Glu Glu Leu Glu Asn Asn Val Asp
     50                  55                  60

Gln Ile Leu Lys Trp Ile Glu Gln Trp Ile Lys Asp His Asn Ser Xaa
 65                  70                  75                  80

<210> 171
```



```
<211> 42
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (42)
<223> Xaa equals stop translation

<400> 171
Met Lys Ile Leu Ile Leu Phe Ile Phe Ile Pro Gly Leu Leu Val Glu
  1               5                  10                  15

Lys Asn Gly Pro Asp His Val Cys Val Cys Met Cys Val Arg Val Cys
             20                  25                  30

Val Cys Ala His Leu Gly Leu Phe Ile Xaa
         35                  40

<210> 172
<211> 131
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (43)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (44)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (49)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (66)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (78)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (94)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (102)
```

<223> Xaa equals any of the naturally occurring L-amino acids

<400> 172
Met Trp Ser Val Ile Arg Ser Leu Cys Pro Ser Arg Leu Gln Ser Leu
1 5 10 15

His Val Cys Phe Cys Pro Arg Leu Cys Leu Ala Val Pro Cys Val Phe
20 25 30

His Leu Ser Ser Pro Trp Phe His Val Arg Xaa Xaa Phe Phe Ser Gly
35 40 45

Xaa Pro Gly Cys Ile Trp Gly Ile Cys Phe Val Gly Leu Leu Leu Gly
50 55 60

Ala Xaa Arg Pro Arg Ser Gly Cys Leu Cys Ser Pro Ser Xaa Cys Leu
65 70 75 80

Trp Ser Leu Val Val Cys Glu Ser Ile Cys Leu Pro Arg Xaa Gly Pro
85 90 95

Asn Gln Ala Pro Pro Xaa Pro Leu Phe Leu Ser Leu Asn Leu Pro Phe
100 105 110

Leu Phe Gln Pro Leu Gln Met Arg Trp Leu Ser Ala Val Gly Trp Arg
115 120 125

Glu Ala Met
130

<210> 173
<211> 45
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (45)
<223> Xaa equals stop translation

<400> 173
Met Gln Leu Ser Leu Ser Leu Cys Ala Phe Val Val Cys Thr Asn Ala
1 5 10 15

Val Cys Thr His Ala Ala Thr Asn Gln Ala Arg Leu Val Gly Phe Leu
20 25 30

Lys Val Leu Arg Pro Ala His Ser Pro Leu Cys Leu Xaa
35 40 45

<210> 174
<211> 63
<212> PRT
<213> Homo sapiens

<220>

<221> SITE
<222> (10)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (25)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (38)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (63)
<223> Xaa equals stop translation

<400> 174
Met Gln Pro Ala Trp Leu Trp Leu Trp Xaa Trp Glu Leu Gly Trp Glu
1 5 10 15

Leu Val Phe Gly Ala Ile Leu Leu Xaa Leu Gln Asp Gly Leu Phe Asp
20 25 30

Ser Val Leu Tyr Cys Xaa His Leu Tyr Ser Gly Leu Phe Phe Pro Trp
35 40 45

Ile Val Asn Ser Leu Met Ser Gly Ser Ser Gln Leu Met Ser Xaa
50 55 60

<210> 175
<211> 20
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (20)
<223> Xaa equals stop translation

<400> 175
Met Ser Ser Pro Lys Ser Leu Val Leu Leu Leu Ala Val Ile Cys Arg
1 5 10 15

Glu Ala Thr Xaa
20

<210> 176
<211> 41
<212> PRT
<213> Homo sapiens

<220>
<221> SITE

<222> (41)
<223> Xaa equals stop translation

<400> 176
Met Asn Ile Val Pro Gln Phe Ser Val Leu Pro His Phe Ala Tyr Phe
1 5 10 15

Ser Phe Ile Ile Leu Tyr Trp Ala Val Leu Phe Ser Gln Thr Ile Cys
20 25 30

Ser Met Ser Val Phe Lys Val Lys Xaa
35 40

<210> 177
<211> 49
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (49)
<223> Xaa equals stop translation

<400> 177
Met Thr Asp Ile Thr Cys Phe Leu Phe Ser Tyr Leu Ser Thr Leu Leu
1 5 10 15

Ser Pro Ile Tyr Leu Asp Val Leu Leu Phe Ser Leu Leu Leu Phe Leu
20 25 30

Phe His Ile Ala Gly Met His Ile Leu Thr Phe Ile Asn His Asp Ile
35 40 45

Xaa

<210> 178
<211> 107
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (59)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (63)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (65)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (77)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (88)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (105)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (107)
<223> Xaa equals stop translation

<400> 178
Met Gly Ala Ala Leu Ala Ala Trp Ile Cys Ile Val Arg Tyr His Gln
1 5 10 15

Leu Arg Asp Trp Gly Val Arg Arg Trp Pro Asn Gln Leu Ile Leu Trp
20 25 30

Thr Gly Leu Leu Cys Ala Leu Gly Thr Ser Val Val Gly Asn Leu Pro
35 40 45

Gly Glu Thr Gln Ser Ala Pro Arg Val Cys Xaa Arg Pro Ala Xaa Gly
50 55 60

Xaa Thr Thr Pro Ser Met Pro Arg Gly His Arg Leu Xaa Val Ser Gly
65 70 75 80

Ala Gly Ser Arg Pro Pro Phe Xaa Gly Leu Val Phe Phe Ser Gly His
85 90 95

Trp Pro Gly Pro Ala Gly Ser Phe Xaa Leu Xaa
100 105

<210> 179
<211> 46
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (46)
<223> Xaa equals stop translation

<400> 179
Met Gly Cys Trp Val Leu Phe Ile Leu Leu Tyr Leu Ala Leu His Ile
1 5 10 15

Cys Val Gln Asn Tyr Ile Tyr Ser Tyr Lys Ile Ile Cys Leu Gln Ser

20 25 30

Phe His Tyr Ile Val Arg Lys Ile Gln Ile Phe Val Ser Xaa
35 40 45

<210> 180
<211> 67
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (67)
<223> Xaa equals stop translation

<400> 180
Met Leu Leu Ala Ala Phe Leu Ala Leu Phe Pro Leu His Asp Ser Arg
1 5 10 15

Gly Leu Lys His Thr Gly Ala Gly His Val Asn Ser Val Ala Leu Leu
20 25 30

Pro Ile Pro Leu Lys Ala Val Ser Leu Ser Pro Val Ser Ser Leu Gln
35 40 45

Val Pro Cys Cys Cys Ser Ser Phe Gln Leu Leu Leu Thr Phe Leu Ser
50 55 60

Val Ser Xaa
65

<210> 181
<211> 50
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (50)
<223> Xaa equals stop translation

<400> 181
Met Ile Cys Lys Phe Leu Ile Ile Ile Cys Ile Thr Leu Leu Leu Phe
1 5 10 15

Ala Ile Cys Gln Leu Cys Lys Arg Gln Gly Leu Val Gln Lys Ile Ser
20 25 30

Phe Tyr Gln Lys Glu Thr Leu Ser Ser Thr Val Gly Thr Thr Phe Leu
35 40 45

Ser Xaa
50

<210> 182

<211> 73
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (35)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (73)
<223> Xaa equals stop translation

<400> 182
Met Leu Thr Trp Val Trp Tyr Leu Ile Met Thr Ser Val Leu Gln Ala
1 5 10 15

Ser Val Ser Ser Val Val Arg Gly Ser Ile Leu Val Gly Gly Ser Glu
20 25 30

Asp Cys Xaa Glu Gly Gly Ser Leu Ile Gln Val Ser Leu Gly Tyr Val
35 40 45

Leu Ala Ala Arg Glu Asp Arg Gln Glu Cys Gly Pro Asp Thr Val Ser
50 55 60

Cys Pro Pro Gly Met Arg Leu Asp Xaa
65 70

<210> 183
<211> 44
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (44)
<223> Xaa equals stop translation

<400> 183
Met Leu Ser Ala Leu Ser Ala Leu Tyr Leu Ile Ile Thr Ile Phe Leu
1 5 10 15

Lys Gly Ser Cys Cys Ser Cys His His Cys Phe Thr Asn Gly Lys Leu
20 25 30

Trp Leu Arg Lys Phe Ile Ser Gly Ser Gln Pro Xaa
35 40

<210> 184
<211> 58
<212> PRT
<213> Homo sapiens

<220>

<221> SITE
<222> (58)
<223> Xaa equals stop translation

<400> 184
Met Cys Met Thr Val Phe Ile Val Phe Tyr Tyr Ser Phe Met Arg Leu
1 5 10 15

Leu Phe Arg Cys Ser His Asn Arg Arg His Trp Arg Gly Ser Gly Lys
20 25 30

Asn Thr Val Tyr His Thr Gly Pro Arg Asp Glu Ala Cys Cys Ala Met
35 40 45

Pro Cys Trp Ala Thr Trp Gly Arg Arg Xaa
50 55

<210> 185
<211> 69
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (69)
<223> Xaa equals stop translation

<400> 185
Met Pro Leu Ala Leu Lys Arg Gly Gln Leu Phe Leu Ile Pro Trp Leu
1 5 10 15

Phe Pro Gln Gly Val Cys Pro Leu Glu Gly Glu Gln Leu Gly Ser Gly
20 25 30

Lys Glu Gly Leu Leu Gln Phe Ala Ile Ala Ser Cys Pro Arg Val Tyr
35 40 45

Pro Glu His Ser Pro Pro Trp Lys Glu Thr Gln Ser Ala Thr Gly Tyr
50 55 60

Arg Lys Ser Asp Xaa
65

<210> 186
<211> 25
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (25)
<223> Xaa equals stop translation

<400> 186
Met Lys Tyr Leu Leu Phe Leu Val Phe Cys Leu Ser Tyr Val Lys Asp
1 5 10 15

Leu Asn Ile Phe Asp Leu Leu Tyr Xaa
20 25

<210> 187
<211> 58
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (58)
<223> Xaa equals stop translation

<400> 187
Met Thr Leu Pro Trp Glu Trp Val Pro Asp Lys Arg Ile Trp Leu Leu
1 5 10 15

Ser Leu Thr Leu Val His Ala Leu Leu Pro Leu Cys Leu Leu Pro Trp
20 25 30

Asp Val Gly Ala Arg Ser Pro Phe Ile Ser Gly Glu Pro Ile Asn Leu
35 40 45

Gly Phe Pro Asn Leu Gln Asn Cys Lys Xaa
50 55

<210> 188
<211> 67
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (67)
<223> Xaa equals stop translation

<400> 188
Met Val Gly Leu Leu Leu Ile Ala Leu Leu Thr Trp Gly Tyr Ile Arg
1 5 10 15

Tyr Ser Gly Gln Tyr Arg Glu Leu Gly Gly Ala Ile Asp Phe Gly Ala
20 25 30

Ala Tyr Val Leu Glu Gln Ala Ser Ser His Ile Gly Asn Ser Thr Gln
35 40 45

Ala Thr Val Arg Asp Ala Val Val Gly Arg Pro Ser Met Asp Lys Lys
50 55 60

Ala Gln Xaa
65

<210> 189
<211> 89

<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (18)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (63)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (89)
<223> Xaa equals stop translation

<400> 189
Met Ser Thr Tyr Leu Lys Met Phe Ala Ala Ser Leu Leu Ala Met Cys
1 5 10 15

Ala Xaa Ala Glu Val Val His Arg Tyr Tyr Arg Pro Asp Leu Met Arg
20 25 30

Asn Arg Leu Arg Arg Val Lys Leu Ile Ser Gln Ser His Ile Ala Leu
35 40 45

Val Arg Arg Phe Glu Asp Leu Lys Pro Lys Leu Ser Val Cys Xaa Thr
50 55 60

Gly Ile Thr Ser Leu Ser Val Gly Glu Leu Glu Val Trp Ala Glu Ser
65 70 75 80

Ser Arg Gly Asp Leu Met Thr Ala Xaa
85

<210> 190
<211> 221
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (159)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (221)
<223> Xaa equals stop translation

<400> 190
Met Lys Leu Leu Leu Trp Ala Cys Ile Val Cys Val Ala Phe Ala Arg
1 5 10 15

Lys Arg Arg Phe Pro Phe Ile Gly Glu Asp Asp Asn Asp Asp Gly His

20 25 30

Pro Leu His Pro Ser Leu Asn Ile Pro Tyr Gly Ile Arg Asn Leu Pro
35 40 45

Pro Pro Leu Tyr Tyr Arg Pro Val Asn Thr Val Pro Ser Tyr Pro Gly
50 55 60

Asn Thr Tyr Thr Asp Thr Gly Leu Pro Ser Tyr Pro Trp Ile Leu Thr
65 70 75 80

Ser Pro Gly Phe Pro Tyr Val Tyr His Ile Arg Gly Phe Pro Leu Ala
85 90 95

Thr Gln Leu Asn Val Pro Pro Leu Pro Pro Arg Gly Phe Pro Phe Val
100 105 110

Pro Pro Ser Arg Phe Phe Ser Ala Ala Ala Ala Pro Ala Ala Pro Pro
115 120 125

Ile Ala Ala Glu Pro Ala Ala Ala Ala Pro Leu Thr Ala Thr Pro Val
130 135 140

Ala Ala Glu Pro Ala Ala Arg Gly Pro Val Ala Ala Glu Pro Xaa Gly
145 150 155 160

Arg Gly His Leu Leu Glu Leu Glu Pro Ala Ala Glu Ala Pro Val Ala
165 170 175

Ala Glu Pro Ala Ala Glu Ala Pro Val Gly Val Glu Pro Ala Ala Glu
180 185 190

Glu Pro Ser Pro Ala Glu Pro Ala Thr Ala Lys Pro Ala Ala Pro Glu
195 200 205

Pro His Pro Ser Pro Ser Leu Glu Gln Ala Asn Gln Xaa
210 215 220

<210> 191
<211> 52
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (52)
<223> Xaa equals stop translation

<400> 191
Met Glu Arg Leu Val Leu Ser Leu Trp Ser Leu Thr Cys Arg Ala Ser
1 5 10 15

Pro Ala Asn Thr His Pro Arg Thr Thr Ser Arg Thr Arg Thr Leu Asp
20 25 30

Val Lys Thr Lys Cys Pro Val Glu Ala Val Lys Leu Ser Glu Met Leu
35 40 45

Pro Pro Val Xaa
50

<210> 192
<211> 72
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (72)
<223> Xaa equals stop translation

<400> 192
Met Val Gly Thr His Leu Ile Leu Phe Pro Phe Leu Leu Arg Thr Met
1 5 10 15

Val Ile Phe Leu Cys Leu Lys Ser Ser Cys Gly Ser Phe Leu Pro Ile
20 25 30

Asn Lys Ile Gln Thr Pro Phe Ile Leu Asn Leu Ile Tyr Lys Thr Phe
35 40 45

Lys Met Cys Ser Leu Pro Asn Ser Leu Phe Ser Pro Leu Ser Phe Ile
50 55 60

Phe Phe Ile Phe Phe Leu Thr Xaa
65 70

<210> 193
<211> 112
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (108)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (112)
<223> Xaa equals stop translation

<400> 193
Met Arg Arg Leu Leu Leu Ala Leu Pro Phe Ala Leu Leu Pro Leu Ala
1 5 10 15

Val Ala His Ala His Glu Asp His Asp His Glu His Gly Ser Leu Gly
20 25 30

Ala His Glu His Gly Val Gly Arg Leu Asn Ala Val Leu Asp Gly Gln
35 40 45

Ala Leu Glu Leu Glu Leu Asp Ser Pro Ala Met Asn Leu Val Gly Phe

50 55 60

Glu His Val Ala Thr Ser Ala Ala Asp Lys Ala Lys Val Ala Ala Val
65 70 75 80

Arg Lys Gln Leu Glu Asn Pro Ser Gly Pro Val Gln Pro Ala Gln Ser
85 90 95

Arg Ser Cys Val Val Ser Asn Gln Gly Ile Asn Xaa Arg Cys Ser Xaa
100 105 110

<210> 194
<211> 61
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (14)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (61)
<223> Xaa equals stop translation

<400> 194
Met Phe Ile Thr Arg Gly Cys Tyr Cys Phe Val Phe Phe Xaa Leu Ala
1 5 10 15

His Asn Cys Lys Ala Ala Arg Thr Thr Arg Asn Gly Phe Pro Thr Val
20 25 30

Pro Gly Arg Arg Gln Arg Thr Leu Arg Arg Leu Phe Leu Cys Gly Phe
35 40 45

Pro Leu Leu Cys Ser Gln Gly Asp Leu Ser Ala Ala Xaa
50 55 60

<210> 195
<211> 126
<212> PRT
<213> Homo sapiens

<400> 195
Met Thr Lys Leu Ala Gln Trp Leu Trp Gly Leu Ala Ile Leu Gly Ser
1 5 10 15

Thr Trp Val Ala Leu Thr Thr Gly Ala Leu Gly Leu Glu Leu Pro Leu
20 25 30

Ser Cys Gln Glu Val Leu Trp Pro Leu Pro Ala Tyr Leu Leu Val Ser
35 40 45

```
Ala Gly Cys Tyr Ala Leu Gly Thr Val Gly Tyr Arg Val Ala Thr Phe
     50                  55                  60

His Asp Cys Glu Asp Ala Ala Arg Glu Leu Gln Ser Gln Ile Gln Glu
 65                  70                  75                  80

Ala Arg Ala Asp Leu Ala Arg Arg Gly Cys Ala Ser Asp Ser Leu Thr
                 85                  90                  95

Pro Phe Leu Cys Gly Gln Pro Phe Leu Pro Phe Pro Ile Lys Glu Pro
            100                 105                 110

Val Tyr Phe Leu Lys Lys Lys Lys Lys Lys Lys Lys Lys Lys
        115                 120                 125
```

<210> 196
<211> 113
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (41)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (109)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (113)
<223> Xaa equals stop translation

<400> 196

```
Met Ala Ala Leu Leu Leu Leu Pro Trp Leu Met Leu Leu Thr Gly Arg
  1               5                  10                  15

Val Ser Leu Ala Gln Phe Ala Leu Ala Phe Val Thr Asp Thr Cys Val
             20                  25                  30

Ala Gly Ala Leu Leu Cys Gly Ala Xaa Leu Leu Phe His Gly Met Leu
         35                  40                  45

Leu Leu Arg Gly Gln Thr Thr Trp Glu Trp Ala Arg Gly Gln His Ser
     50                  55                  60

Tyr Asp Leu Gly Pro Cys His Asn Leu Gln Ala Ala Leu Gly Pro Arg
 65                  70                  75                  80

Trp Ala Leu Val Trp Leu Trp Pro Phe Leu Ala Ser Pro Leu Pro Gly
                 85                  90                  95

Asp Gly Ile Thr Phe Gln Thr Thr Ala Asp Val Gly Xaa Thr Ala Ser
            100                 105                 110
```


Xaa

<210> 197
<211> 66
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (66)
<223> Xaa equals stop translation

<400> 197

```
Met Leu Gly Ile Thr Arg Leu Trp Val Leu Leu Lys Pro Cys Phe Pro
  1               5                  10                  15

Arg Cys Tyr Ser Ser Thr Gly Gly Glu Val Leu Pro Arg Cys Cys Glu
             20                  25                  30

Val Glu Ala Glu Val Gln Val Pro His Ser Ala Pro Met Asp Ser Arg
         35                  40                  45

Glu Gly Gly Thr Val Pro Tyr Phe Gly Gly Cys Gly Ser Pro Arg Phe
     50                  55                  60

Tyr Xaa
 65
```

<210> 198
<211> 52
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (23)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (52)
<223> Xaa equals stop translation

<400> 198

```
Met Ala Gln His His Leu Leu Ser Ile Leu Leu Ala Ile Leu Ser Cys
  1               5                  10                  15

Ser Ser Gln Pro Arg Gln Xaa Arg Gly Ser Gly Ala Leu Pro Cys Glu
             20                  25                  30

Val Cys Ser Ala Val Leu Leu Thr Cys Leu Arg Lys Ile Ser Gly Ser
         35                  40                  45

Leu Cys Val Xaa
```

50

<210> 199
<211> 59
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (59)
<223> Xaa equals stop translation

<400> 199
Met Ile Gly Lys Ser Leu Val Met Phe Cys Phe Leu Ser Trp Gly Ala
1 5 10 15

Gly Val His Gly Cys Ala Leu Tyr Tyr Asn Ala Ser Asn Arg Ile Gly
20 25 30

Ile Phe Tyr Ile Phe Cys Phe Thr Tyr Leu Arg Leu His Glu Cys Val
35 40 45

Met Leu Ser Asn Leu Arg Val Asn Glu Leu Xaa
50 55

<210> 200
<211> 52
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (52)
<223> Xaa equals stop translation

<400> 200
Met Leu Ser Pro Leu Ser Gln Ser Leu Leu Val Ala Leu Asn Val Leu
1 5 10 15

Phe Leu Leu Pro Asn Phe Leu Ala Leu Ser Lys Asn Leu Thr Tyr Asp
20 25 30

Cys Tyr Phe Arg Phe Phe Pro Thr Phe Phe Leu Pro Pro Lys Glu Met
35 40 45

Trp Tyr Leu Xaa
50

<210> 201
<211> 81
<212> PRT
<213> Homo sapiens

<220>
<221> SITE

<222> (81)
<223> Xaa equals stop translation

<400> 201
Met Cys Pro Ala Ala Ala Leu Ala Trp Pro Thr Ser Ala Ile Ser Leu
1 5 10 15

Ile Val Ser Leu Ala Pro Ser Trp Ala Ala Ala Arg Asp Asn Trp Ala
20 25 30

Ala Ser Pro Tyr Thr Thr Gln Ala Arg Pro Ala Leu Arg Ala Ala Leu
35 40 45

Thr Thr Ile Ser Gly Pro Met Pro Ala Ala Ser Pro Met Val Met Pro
50 55 60

Thr Gly Arg Glu Gly Phe Thr Val Leu Gly Met Gly Leu Arg Cys Gly
65 70 75 80

Xaa

<210> 202
<211> 70
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (70)
<223> Xaa equals stop translation

<400> 202
Met Phe Leu Ile Val Phe Cys Phe Leu Gln Ser Leu Ser Ala Met Pro
1 5 10 15

Ile Val Leu Ile Phe Tyr Arg Ser Ser Leu Lys Ile Leu Asn Arg Gly
20 25 30

Ile Gly Ser Gly Gln Ser Glu Trp Leu Glu Phe Trp Leu Ser Lys Lys
35 40 45

Asn Phe Ile Leu His Lys His Val Val Arg Ser Phe Cys Ala Tyr Ala
50 55 60

Ala Trp Ile Gly Cys Xaa
65 70

<210> 203
<211> 46
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (46)

<223> Xaa equals stop translation

<400> 203
Met Leu Leu Cys Ser Val Arg Asn Ile Leu Trp His Thr Ala Phe Leu
1 5 10 15

Gly Ser Ala Val Leu Cys Phe Val Leu Val Leu Val Leu His Leu Glu
20 25 30

Cys Leu Ile Ile Asp Ala Tyr Phe Asn Ser Ile Ser Phe Xaa
35 40 45

<210> 204
<211> 53
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (53)
<223> Xaa equals stop translation

<400> 204
Met Gly Thr Glu Ala Ser Pro Lys Arg Tyr Phe Phe Val Val Val Val
1 5 10 15

Val Leu Gly Ile Ile Val Pro Ile Leu Arg Ala Phe Pro Pro Pro Val
20 25 30

Pro Thr His Pro Asn Lys Met Trp Trp Cys Cys Leu Gln Lys Arg Glu
35 40 45

Val Leu Cys His Xaa
50

<210> 205
<211> 62
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (62)
<223> Xaa equals stop translation

<400> 205
Met Phe Cys Trp Ile Leu Val Cys Leu Ala Tyr Leu Lys Val Pro Leu
1 5 10 15

Leu Phe Phe Phe Phe Phe Phe Leu Ser Ala Leu Phe Cys Arg Thr Cys
20 25 30

Ser Asn Met Glu Asn Lys Ser Arg Arg Leu Ser Ser Asp Cys Tyr Leu
35 40 45

Cys Pro Lys Pro Pro Gln Thr Phe Met Leu Met Phe Tyr Xaa

50 55 60

<210> 206
<211> 44
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (44)
<223> Xaa equals stop translation

<400> 206
Met Leu Phe Leu His Thr Arg Leu His Phe Pro Arg Tyr Thr Leu Leu
1 5 10 15

Ile Cys Lys Val Leu Leu Val Val Ala Ala Ser Val His Arg Pro Trp
20 25 30

Leu Arg Ser Ile Thr Gly Cys Phe Phe Thr Lys Xaa
35 40

<210> 207
<211> 41
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (41)
<223> Xaa equals stop translation

<400> 207
Met Ser Ala Ser Leu Cys Leu Phe Thr Gln Val Leu Lys Gly Ile Val
1 5 10 15

Trp Leu Pro Ile Leu Met Phe His Val Gly Ala Thr Lys Thr Ser Gly
20 25 30

Phe Ser Val Glu Gln Leu Tyr Ser Xaa
35 40

<210> 208
<211> 57
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (57)
<223> Xaa equals stop translation

<400> 208
Met Phe Lys Arg Met Cys Phe Phe Phe Gln Val Phe Leu Pro Leu Ala
1 5 10 15

```
Cys Thr Glu Leu Leu Trp Lys Gly Ala Pro Cys Arg His Ile Phe Gln
            20                  25                  30

Thr Gly Pro Asp Leu Leu Val Thr Gln Arg Cys Val His Ser Leu Leu
        35                  40                  45

Leu Gly Tyr Leu Ile Ser Ile Phe Xaa
    50                  55
```

<210> 209
<211> 126
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (126)
<223> Xaa equals stop translation

<400> 209

```
Met Met Thr Gln Thr Cys Ile Ile Leu Leu Ile His Thr Met Gln Val
  1               5                  10                  15

Cys Thr Thr His Pro Thr Val Leu Ser His Thr Leu Leu Gln Arg Pro
            20                  25                  30

Lys Pro Thr Asp Leu Phe Pro Lys Ala Thr Pro Thr Thr Ala Pro Met
        35                  40                  45

Pro Leu Arg Met Arg Pro Pro Gln Cys Leu Pro His Met Phe His Leu
    50                  55                  60

Gln Ser Arg Arg Phe Asp Gln Glu Ile Gly Leu Gln Gln Lys Ser Met
 65                  70                  75                  80

Thr Gly Ile Leu Gln Thr Glu Lys Trp Thr Gln Glu Asn Phe Gly Leu
                85                  90                  95

Ser Gln Gly Val Phe Leu Asn Met Asn Leu Ala Ser His Gln Phe Phe
            100                 105                 110

Ser Met Lys Asp Gln Leu Pro Ser Leu Lys Leu Pro Asp Xaa
        115                 120                 125
```

<210> 210
<211> 26
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (26)
<223> Xaa equals stop translation

<400> 210


```
Met Val Asn Ile Phe Gly Phe Val Ser Cys Ile Val Phe Val Val Ala
  1               5                  10                  15

Val Gln Leu Cys Tyr Met Lys Gln Pro Xaa
            20                  25
```

<210> 211
<211> 48
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (48)
<223> Xaa equals stop translation

<400> 211

```
Met Leu Gln Phe Leu Leu Gly Phe Thr Leu Gly Asn Val Val Gly Met
  1               5                  10                  15

Tyr Leu Ala Gln Asn Tyr Asp Ile Pro Asn Leu Ala Lys Lys Leu Glu
            20                  25                  30

Glu Ile Lys Lys Asp Leu Asp Ala Lys Lys Lys Pro Pro Ser Ala Xaa
        35                  40                  45
```

<210> 212
<211> 45
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (45)
<223> Xaa equals stop translation

<400> 212

```
Met Ala Ser Gly Ser Trp Thr Ser Ala Pro Gly Ile Gly Val Ile Leu
  1               5                  10                  15

Val Met Thr Val Cys Leu Ser His Cys Tyr Thr His Glu Trp Gly Leu
            20                  25                  30

Trp Gly Gly Gly Gly Thr Gln Gly Leu Thr Asp Ser Xaa
        35                  40                  45
```

<210> 213
<211> 52
<212> PRT
<213> Homo sapiens

<220>

<221> SITE
<222> (52)
<223> Xaa equals stop translation

<400> 213
Met Tyr Ile Leu Cys Ser Gly Leu Leu Gln Gly Gln Leu His Tyr Phe
1 5 10 15

Leu Gly Trp Ala Phe Leu Trp Leu Lys Leu Gly Cys Pro Trp Leu Ser
20 25 30

Gln Gly Ser Gln Pro Lys Arg His Ser Gly Glu Asn Leu Trp Pro Ile
35 40 45

Arg Glu Glu Xaa
50

<210> 214
<211> 51
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (51)
<223> Xaa equals stop translation

<400> 214
Met Tyr Ser Leu Val Leu Thr Phe Leu Val Ser Phe Cys Ala Leu Ser
1 5 10 15

Lys Thr Phe Leu Asp His Trp Phe Gln Met Phe Ile Tyr Tyr Ile Leu
20 25 30

Phe Lys Asp Ser Glu Ile Gly Phe Cys His Pro Leu Leu Tyr Val Leu
35 40 45

Phe His Xaa
50

<210> 215
<211> 210
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (135)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (143)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE
<222> (179)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (182)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (210)
<223> Xaa equals stop translation

<400> 215
Met Arg Ser Thr Ile Leu Leu Phe Cys Leu Leu Gly Ser Thr Arg Ser
1 5 10 15

Leu Pro Gln Leu Lys Pro Ala Leu Gly Leu Pro Pro Thr Lys Leu Ala
20 25 30

Pro Asp Gln Gly Thr Leu Pro Asn Gln Gln Gln Ser Asn Gln Val Phe
35 40 45

Pro Ser Leu Ser Leu Ile Pro Leu Thr Gln Met Leu Thr Leu Gly Pro
50 55 60

Asp Leu His Leu Leu Asn Pro Ala Ala Gly Met Thr Pro Gly Thr Gln
65 70 75 80

Thr His Pro Leu Thr Leu Gly Gly Leu Asn Val Gln Gln Gln Leu His
85 90 95

Pro His Val Leu Pro Ile Phe Val Thr Gln Leu Gly Ala Gln Gly Thr
100 105 110

Ile Leu Ser Ser Glu Glu Leu Pro Gln Ile Phe Thr Ser Leu Ile Ile
115 120 125

His Ser Leu Phe Pro Gly Xaa Ile Leu Pro Thr Ser Gln Ala Xaa Ala
130 135 140

Asn Pro Asp Val Gln Asp Gly Ser Leu Pro Ala Gly Gly Ala Gly Val
145 150 155 160

Asn Pro Ala Thr Gln Gly Thr Pro Ala Gly Arg Leu Pro Thr Pro Ser
165 170 175

Gly Thr Xaa Asp Asp Xaa Ala Val Thr Thr Pro Ala Gly Ile Gln Arg
180 185 190

Ser Thr His Ala Ile Glu Glu Ala Thr Thr Glu Ser Ala Asn Gly Ile
195 200 205

Gln Xaa
210

<210> 216
<211> 195
<212> PRT
<213> Homo sapiens

<400> 216
Met Ala Pro Ala Ala Ser Arg Leu Arg Ala Glu Ala Gly Leu Gly Ala
1 5 10 15

Leu Pro Arg Arg Ala Leu Ala Gln Tyr Leu Leu Phe Leu Arg Leu Tyr
20 25 30

Pro Val Leu Thr Lys Ala Ala Thr Ser Gly Ile Leu Ser Ala Leu Gly
35 40 45

Asn Phe Leu Ala Gln Met Ile Glu Lys Lys Arg Lys Lys Glu Asn Ser
50 55 60

Arg Ser Leu Asp Val Gly Gly Pro Leu Arg Tyr Ala Val Tyr Gly Phe
65 70 75 80

Phe Phe Thr Gly Pro Leu Ser His Phe Phe Tyr Phe Phe Met Glu His
85 90 95

Trp Ile Pro Pro Glu Val Pro Leu Ala Gly Leu Arg Arg Leu Leu Leu
100 105 110

Asp Arg Leu Val Phe Ala Pro Ala Phe Leu Met Leu Phe Phe Leu Ile
115 120 125

Met Asn Phe Leu Glu Gly Lys Asp Ala Ser Ala Phe Ala Ala Lys Met
130 135 140

Arg Gly Gly Phe Trp Pro Ala Leu Arg Met Asn Trp Arg Val Trp Thr
145 150 155 160

Pro Leu Gln Phe Ile Asn Ile Asn Tyr Val Pro Leu Lys Phe Arg Val
165 170 175

Leu Phe Ala Asn Leu Ala Ala Leu Phe Trp Tyr Ala Tyr Leu Ala Ser
180 185 190

Leu Gly Lys
195

<210> 217
<211> 35
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (35)
<223> Xaa equals stop translation

<400> 217
Met Gln Ala Arg Trp Phe His Ile Leu Gly Met Met Met Phe Ile Trp

1 5 10 15

Ser Ser Ala His Gln Tyr Lys Cys Pro Cys Tyr Ser Arg Gln Ser Gln
20 25 30

Glu Lys Xaa
35

<210> 218
<211> 72
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (72)
<223> Xaa equals stop translation

<400> 218
Met Phe Pro Ser Cys Leu Pro Leu Leu Phe Asn Ala Lys Val Leu Ala
1 5 10 15

Lys Asp Ile Phe Leu Leu Leu Leu Cys Phe Ser Ile Leu Phe Cys Thr
20 25 30

Val Gly Trp Leu Ser Ala Pro Thr Leu Gly Thr Gly Pro Trp Leu Gly
35 40 45

His Phe Met Ala Gln Ser Leu Trp Gly Leu Lys Glu Gly Trp Ala Ala
50 55 60

Gln Ser Leu His Gly Ser Cys Xaa
65 70

<210> 219
<211> 53
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (53)
<223> Xaa equals stop translation

<400> 219
Met Ala Val Ser Leu Trp Pro Glu Gly Ser Gly Pro Leu Cys Ala Leu
1 5 10 15

Ser Leu Leu Thr Cys Cys Leu Val Leu Arg Pro Ala Ser Ser Ser Gly
20 25 30

Phe Leu Trp Ser Leu Glu Glu Thr Pro Ala Leu Gln Gly Leu Cys Glu
35 40 45

Ile Ala Gln Pro Xaa
50

<210> 220
<211> 69
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (69)
<223> Xaa equals stop translation

<400> 220
Met Val His Asn Cys Leu Leu Leu Leu Lys Phe Leu Leu Leu Phe Cys
1 5 10 15

Phe Pro Leu Ile Ser Tyr Gln Leu Met Asn Gly Ser Leu Gln Ser Leu
20 25 30

Gln Arg Leu Arg Met Ile Gln Asn Val Gln Cys Ile Val Leu Asn Lys
35 40 45

Gln Glu Ala Glu Phe Leu Met Gly Ile Ser Phe Gln Ile Tyr Asp Trp
50 55 60

Ser Leu Gly Phe Xaa
65

<210> 221
<211> 69
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (69)
<223> Xaa equals stop translation

<400> 221
Met Ser His Leu Gln Thr Leu His Leu Ile Gly Leu Ser Cys Ser Phe
1 5 10 15

Leu Tyr Phe Pro Thr Ser Gln Ala Val Glu Ala Ala Glu Pro Gly Met
20 25 30

Met Leu Ser Leu Arg Gln Met Thr Asn Pro Leu Val Ala Arg Asn Gln
35 40 45

Thr Ala Pro Arg Ala Gly Val Ser Val Phe Cys Thr Asp Cys Leu Phe
50 55 60

Gly Leu Asp Ile Xaa
65

<210> 222
<211> 44

<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (44)
<223> Xaa equals stop translation

<400> 222
Met Leu Thr Cys Ile Asp Met Asp Trp Lys Val Leu Thr Trp Leu Arg
1 5 10 15

Tyr Thr Leu Trp Ile Pro Leu Tyr Pro Leu Gly Met Phe Gly Gly Ser
20 25 30

Cys Leu Ser Asp Ser Val His Ser Asn Ile Gln Xaa
35 40

<210> 223
<211> 103
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (103)
<223> Xaa equals stop translation

<400> 223
Met Trp Ser Ser Ile Arg Leu Leu Ser Pro Val Leu Ser Leu Ile Leu
1 5 10 15

Leu Leu Ile Ala Leu Glu Leu Val Asn Ile His Ala Val Cys Gly Lys
20 25 30

Asn Ala His Glu Tyr Gln Gln Tyr Leu Lys Phe Val Lys Ser Ile Leu
35 40 45

Gln Tyr Thr Glu Asn Leu Val Ala Tyr Thr Ser Tyr Glu Lys Asn Lys
50 55 60

Trp Asn Glu Thr Ile Asn Leu Thr His Thr Ala Leu Leu Lys Met Trp
65 70 75 80

Thr Phe Ser Glu Lys Lys Gln Met Leu Ile His Leu Ala Lys Lys Ser
85 90 95

Thr Ser Lys Val Leu Leu Xaa
100

<210> 224
<211> 214
<212> PRT
<213> Homo sapiens

<220>

<221> SITE
<222> (214)
<223> Xaa equals stop translation

<400> 224
Met Lys Gly Phe Ser Trp Ala Ile Val Pro Ala Leu Thr Ser Leu Gly
1 5 10 15

Tyr Leu Ile Ile Leu Val Val Ser Ile Phe Pro Phe Trp Val Arg Leu
20 25 30

Thr Asn Glu Glu Ser His Glu Val Phe Phe Ser Gly Leu Phe Glu Asn
35 40 45

Cys Phe Asn Ala Lys Cys Trp Lys Pro Arg Pro Leu Ser Ile Tyr Ile
50 55 60

Ile Leu Gly Arg Val Phe Leu Leu Ser Ala Val Phe Leu Ala Phe Val
65 70 75 80

Thr Thr Phe Ile Met Met Pro Phe Ala Ser Glu Phe Phe Pro Arg Thr
85 90 95

Trp Lys Gln Asn Phe Val Leu Ala Cys Ile Ser Phe Phe Thr Gly Ala
100 105 110

Cys Ala Phe Leu Ala Leu Val Leu His Ala Leu Glu Ile Lys Ala Leu
115 120 125

Arg Met Lys Leu Gly Pro Leu Gln Phe Ser Val Leu Trp Pro Tyr Tyr
130 135 140

Val Leu Gly Phe Gly Ile Phe Leu Phe Ile Val Ala Gly Thr Ile Cys
145 150 155 160

Leu Ile Gln Glu Met Val Cys Pro Cys Trp His Leu Leu Ser Thr Ser
165 170 175

Gln Ser Met Glu Glu Asp His Gly Ser Leu Tyr Leu Asp Asn Leu Glu
180 185 190

Ser Leu Gly Gly Glu Pro Ser Ser Val Gln Lys Glu Thr Gln Val Thr
195 200 205

Ala Glu Thr Val Ile Xaa
210

<210> 225
<211> 109
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (34)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (48)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (109)
<223> Xaa equals stop translation

<400> 225
Met Thr Val Ser Gly Thr Val Val Leu Val Ala Gly Thr Leu Cys Phe
1 5 10 15

Ala Trp Trp Ser Glu Gly Asp Ala Thr Ala Gln Pro Gly Gln Leu Ala
20 25 30

Pro Xaa Thr Glu Tyr Pro Val Pro Glu Gly Pro Ser Pro Leu Leu Xaa
35 40 45

Ser Val Ser Phe Val Cys Cys Gly Ala Gly Gly Leu Leu Leu Leu Ile
50 55 60

Gly Leu Leu Trp Ser Val Lys Ala Ser Ile Pro Gly Pro Pro Ser Met
65 70 75 80

Gly Pro Leu Ser Pro Leu Gln Arg Pro Val Leu Pro His Cys Gly Val
85 90 95

Leu Arg Glu Gly Glu Leu Gln Asp Pro Gln Ser Gly Xaa
100 105

<210> 226
<211> 316
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (316)
<223> Xaa equals stop translation

<400> 226
Met Glu Ser Leu Tyr Asp Leu Trp Glu Phe Tyr Leu Pro Tyr Leu Tyr
1 5 10 15

Ser Cys Ile Ser Leu Met Gly Cys Leu Leu Leu Leu Leu Cys Thr Pro
20 25 30

Val Gly Leu Ser Arg Met Phe Thr Val Met Gly Gln Leu Leu Val Lys
35 40 45

Pro Thr Ile Leu Glu Asp Leu Asp Glu Gln Ile Tyr Ile Ile Thr Leu
50 55 60

Glu Glu Glu Ala Leu Gln Arg Arg Leu Asn Gly Leu Ser Ser Ser Val
65 70 75 80

```
Glu Tyr Asn Ile Met Glu Leu Glu Gln Glu Leu Glu Asn Val Lys Thr
                85                  90                  95

Leu Lys Thr Lys Leu Asp Pro Trp Ser Ser Phe Ser Val Leu Gln Ser
            100                 105                 110

Pro Val Trp His Phe Ala Ala Gln Thr Pro Ala Asp Ile Val Ser Pro
        115                 120                 125

Asp Ser His Phe Met Leu Ser Thr Gln Gly Met Ser Trp Ala Gln Leu
    130                 135                 140

Val Phe Leu Leu Pro Ala Ser Arg Pro Gly Asn Ser Gln Asp Lys Arg
145                 150                 155                 160

Arg Lys Lys Ala Ser Ala Trp Glu Arg Asn Leu Val Tyr Pro Ala Val
                165                 170                 175

Met Val Leu Leu Leu Ile Glu Thr Ser Ile Ser Val Leu Leu Val Ala
            180                 185                 190

Cys Asn Ile Leu Cys Leu Leu Val Asp Glu Thr Ala Met Pro Lys Gly
        195                 200                 205

Thr Arg Gly Pro Gly Ile Gly Asn Ala Ser Leu Ser Thr Phe Gly Phe
    210                 215                 220

Val Gly Ala Ala Leu Glu Ile Ile Leu Ile Phe Tyr Leu Met Val Ser
225                 230                 235                 240

Ser Val Val Gly Phe Tyr Ser Leu Arg Phe Phe Gly Asn Phe Thr Pro
                245                 250                 255

Lys Lys Asp Asp Thr Thr Met Thr Lys Ile Ile Gly Asn Cys Val Ser
            260                 265                 270

Ile Leu Val Leu Ser Ser Ala Leu Pro Val Met Ser Arg Thr Leu Gly
        275                 280                 285

Leu His Lys Leu His Leu Pro Asn Thr Ser Arg Asp Ser Glu Thr Ala
    290                 295                 300

Lys Pro Ser Val Asn Gly His Gln Lys Ala Leu Xaa
305                 310                 315
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<210> 227
<211> 116
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (116)
<223> Xaa equals stop translation

<400> 227


```
Met Leu Ala Leu Ser Ser Ser Phe Leu Val Leu Ser Tyr Leu Leu Thr
 1               5                  10                  15

Arg Trp Cys Gly Ser Val Gly Phe Ile Leu Ala Asn Cys Phe Asn Met
            20                  25                  30

Gly Ile Arg Ile Thr Gln Ser Leu Cys Phe Ile His Arg Tyr Tyr Arg
        35                  40                  45

Arg Ala Pro Thr Gly Pro Trp Leu Ala Cys Thr Tyr Arg Gln Ser Cys
    50                  55                  60

Ser Gly His Leu Pro Ser Val Val Gly Leu Leu Leu Phe Arg Arg Tyr
65                  70                  75                  80

Ser Ser Ala Val Ser Arg Ala Gly Gln Pro Asp Trp His Thr Leu Leu
                85                  90                  95

Trp Gly Pro Ser Val Trp Glu Gln Leu Ser Gly Gln His Ser Ser Gln
            100                 105                 110

Arg Pro Ser Xaa
        115
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<210> 228
<211> 107
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (107)
<223> Xaa equals stop translation

<400> 228

```
Met Cys Val Gly Trp Trp Trp Trp Leu Val Val Leu Gly Leu Gly Met
 1               5                  10                  15

Gly Gly Thr Leu Gly Cys Asp Gly Phe Leu Ser Gln Arg Trp Cys Phe
            20                  25                  30

Thr Ala Gly Lys Tyr Leu Glu Leu Gly Gly Gly Leu Ser Arg His Gln
        35                  40                  45

Ala Asp Phe Ile Phe Ser Gln Thr Lys Ala Thr Phe Thr Ser Lys Gly
    50                  55                  60

Lys Thr Gln Asn Thr Lys Ile Glu Thr Ser Met Pro Pro His Leu Phe
65                  70                  75                  80

Arg Gln Gln Glu Pro Pro Gly Gln Arg Val Phe Leu Thr Leu Arg Val
                85                  90                  95

Thr Leu Thr Ser His Leu Val Ser Cys Gly Xaa
            100                 105
```

<210> 229
<211> 38
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (38)
<223> Xaa equals stop translation

<400> 229
Met Ser Ser Phe Thr Leu Gly Leu Leu Phe Leu Phe Ile Phe Thr Thr
1 5 10 15

Ala Glu Asn Tyr Leu Ile Leu Phe Gln Arg Lys Tyr Cys Leu Val Ile
20 25 30

Phe Trp Gly Glu Phe Xaa
35

<210> 230
<211> 68
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (68)
<223> Xaa equals stop translation

<400> 230
Met Gln Thr Ser Gln Gln Leu Cys Cys Leu Ala Ile Ser Ile Leu Ala
1 5 10 15

Thr Leu Leu Pro Ser Gly Ala Ser Glu Glu Arg Ser Gly Leu Arg Pro
20 25 30

Gly Met Arg Leu Gln Glu Arg Glu Gln Arg Arg Ala Thr Phe Gly Ala
35 40 45

Ser Val His Ser Ser Phe Ile Ser Phe Cys Leu Leu His Gly Val Leu
50 55 60

Asn Lys Phe Xaa
65

<210> 231
<211> 51
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (51)
<223> Xaa equals stop translation

<400> 231
Met Glu Leu Ser Leu Ala Val Leu Glu Ala Val Cys Gln Cys Leu Leu
1 5 10 15

Gly Leu Trp Leu Leu Phe Trp Leu Asp Lys Glu Val Ala Val Phe Val
20 25 30

Leu Leu Leu Trp Leu Phe Thr Asp Leu Thr Asp Val Thr Gly Asp Glu
35 40 45

Cys Arg Xaa
50

<210> 232
<211> 41
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (41)
<223> Xaa equals stop translation

<400> 232
Met Lys Leu Leu Phe Cys Leu Arg Tyr Tyr Met Leu Leu Ser Val Val
1 5 10 15

Val Lys Ala Thr Ser Thr Ile Pro Ser Asn Ile Glu Ile Thr Ser Leu
20 25 30

Ser Trp Val Cys His Asn Ser Thr Xaa
35 40

<210> 233
<211> 42
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (42)
<223> Xaa equals stop translation

<400> 233
Met Arg Leu Val Ser Pro Gly Phe Trp Trp Val Leu Pro Leu Arg Leu
1 5 10 15

Gly Glu Ala Leu Pro Gly Arg Arg Arg Gln Gln Pro Pro Gly Ala Met
20 25 30

Lys Thr Leu Arg Leu Arg Glu Val Lys Xaa
35 40

<210> 234
<211> 48

<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (48)
<223> Xaa equals stop translation

<400> 234
Met Trp Gly Pro Phe Cys Pro Phe Leu Phe Leu Phe Ser Arg Leu Ser
1 5 10 15

Asn Ser Leu Thr Lys Asp Ser Met Asn Ile Lys Ala His Ile His Met
20 25 30

Leu Leu Glu Val Arg Ala Ala His Pro Thr Thr Arg Leu Cys Val Xaa
35 40 45

<210> 235
<211> 40
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (40)
<223> Xaa equals stop translation

<400> 235
Met Phe Ile Leu Ala Ile Trp Asn Phe Phe Ile Leu Tyr Leu Phe Ser
1 5 10 15

Thr Val Ala Gly Leu Val Cys Lys Ser Leu Cys Gln Asn Gln Thr Ile
20 25 30

Phe Lys Thr Ala Leu Cys Phe Xaa
35 40

<210> 236
<211> 64
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (64)
<223> Xaa equals stop translation

<400> 236
Met Leu Arg Gly Trp Ala Leu Ser Thr Phe Leu Val Cys Ile Leu Gln
1 5 10 15

Trp Val Arg Ser Leu Thr Ile Arg Leu Ala Ser Ala Leu Ser Val Arg

20 25 30

Gly Pro Ser Ser Ile Pro Ala Ser Leu Ala Ile Ile Tyr Thr Leu Phe
35 40 45

Ile Phe Ser Phe Lys Phe Leu Lys Ile Val Lys Ser Ile Tyr Ile Xaa
50 55 60

<210> 237
<211> 61
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (61)
<223> Xaa equals stop translation

<400> 237
Met Arg Lys Val Thr Ile Ser Lys Lys His Ala Leu Leu Leu Cys Phe
1 5 10 15

Gln Leu Phe Arg Cys Leu Leu Ser Met Tyr Ile Trp Ile Thr Phe Val
20 25 30

Leu Asp Gly Ser Cys Gly Ile His Cys Ser Leu Lys Pro Val Ser Phe
35 40 45

Pro Cys Thr Tyr His Ser Val His Ser Ser Thr Ser Xaa
50 55 60

<210> 238
<211> 63
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (63)
<223> Xaa equals stop translation

<400> 238
Met Cys Ala Leu Gly Val Phe Leu Leu Val Pro Trp Tyr Glu Tyr Tyr
1 5 10 15

Leu Val Leu Leu Phe Phe Pro Cys Val Ala Phe Ser Val Val Ser Gly
20 25 30

Phe Phe Leu Cys Asn Asp Ser Lys Arg Thr Leu His Ser Cys Ala Leu
35 40 45

Cys Leu Cys Ala Gly Ile Cys Phe Pro Tyr Met Phe Leu Phe Xaa
50 55 60

<210> 239
<211> 57
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (5)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (11)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (45)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (57)
<223> Xaa equals stop translation

<400> 239
Met Met Leu His Xaa Lys Leu Leu Leu Phe Xaa Glu Ala Leu Trp Tyr
1 5 10 15

Tyr Gly Gly Gly Ala Phe Leu Cys Cys Ala Gly Ser Val Pro Thr Asp
20 25 30

Cys Tyr Phe Gly Gly Leu Asp Gln Arg Arg Leu Val Xaa Asp Lys Cys
35 40 45

Thr Glu Lys Ser Thr Gly Leu Leu Xaa
50 55

<210> 240
<211> 182
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (182)
<223> Xaa equals stop translation

<400> 240
Met Thr Val Ile Leu Ile Ile Leu Ile Val Val Met Ala Arg Tyr Cys
1 5 10 15

Arg Ser Lys Asn Lys Asn Gly Tyr Glu Ala Gly Lys Lys Asp His Glu
20 25 30

Asp Phe Phe Thr Pro Gln Gln His Asp Lys Ser Lys Lys Pro Lys Lys
35 40 45

Asp Lys Lys Asn Lys Lys Ser Lys Gln Pro Leu Tyr Ser Ser Ile Val
50 55 60

Thr Val Glu Ala Ser Lys Pro Asn Gly Gln Arg Tyr Asp Ser Val Asn
65 70 75 80

Glu Lys Leu Ser Asp Ser Pro Ser Met Gly Arg Tyr Arg Ser Val Asn
85 90 95

Gly Gly Pro Gly Ser Pro Asp Leu Ala Arg His Tyr Lys Ser Ser Ser
100 105 110

Pro Leu Pro Thr Val Gln Leu His Pro Gln Ser Pro Thr Ala Gly Lys
115 120 125

Lys His Gln Ala Val Gln Asp Leu Pro Pro Ala Asn Thr Phe Val Gly
130 135 140

Ala Gly Asp Asn Ile Ser Ile Gly Ser Asp His Cys Ser Glu Tyr Ser
145 150 155 160

Cys Gln Thr Asn Asn Lys Tyr Ser Lys Gln Met Arg Leu His Pro Tyr
165 170 175

Ile Thr Val Phe Gly Xaa
180

<210> 241
<211> 71
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (71)
<223> Xaa equals stop translation

<400> 241
Met His Met Tyr Val Trp Val Arg Ala His Leu Val Phe Tyr Leu Phe
1 5 10 15

Val Cys Leu Ser Glu Ser Ser Ala Gly Gln Arg Leu Pro Leu Asp Cys
20 25 30

Cys Cys Ser Gly Asp Glu Lys Asp Glu Glu Ser Ala Gly Lys Arg Gly
35 40 45

Gly Val Gln Glu His Gly Gly His Leu Gly Pro Ser Phe Trp His Thr
50 55 60

Lys Pro Glu Phe Ser Cys Xaa
65 70

<210> 242
<211> 62
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (62)
<223> Xaa equals stop translation

<400> 242
Met Trp Arg Val Met Leu Ala Trp Leu Ala Met Val Asn Ser Pro Met
1 5 10 15

Ala Met Glu Ser Gln Val Gly His Ile Ile Ala Val Lys Asp Thr Leu
20 25 30

Thr Gln Met Thr Leu Pro Gly Ala Arg Ile Glu Pro Val Arg Lys Glu
35 40 45

Ser Lys Ala Gly Ser Ala Gly Lys Arg Glu Gly Phe Cys Xaa
50 55 60

<210> 243
<211> 35
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (35)
<223> Xaa equals stop translation

<400> 243
Met Ile Ala Asp Trp Met Phe Phe Val Tyr Ala Leu Cys Ile Asp Val
1 5 10 15

Thr Ala Asn Glu Phe Cys Leu Thr Leu Thr Phe Leu Thr Ser Lys Val
20 25 30

Ser Lys Xaa
35

<210> 244
<211> 47
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (47)
<223> Xaa equals stop translation

<400> 244
Met Glu Pro Val Ala Leu Leu Gln Pro Thr Trp Trp Leu Leu Asn Val
1 5 10 15

Thr Leu Pro Leu Val Ala Trp Ser Gly Pro Leu Ile Cys Arg Pro Leu
20 25 30

Leu His Gly Glu Gly Arg Gln Gly Ala Ala Cys Leu Gln Gly Xaa
35 40 45

<210> 245
<211> 51
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (51)
<223> Xaa equals stop translation

<400> 245
Met His Phe Lys Arg Thr Gln Asn His Leu Asn Ile Val Thr Trp Leu
1 5 10 15

Leu Gln Val Met Ile Ile Val Met Leu Ile Ile Met Arg Ile Ser Cys
20 25 30

Thr His Gln Pro Val Glu Ser Lys Lys Phe Pro Phe Arg Asn Phe Leu
35 40 45

Ser Cys Xaa
50

<210> 246
<211> 51
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (51)
<223> Xaa equals stop translation

<400> 246
Met Thr Tyr His Val Val Cys Ala Phe Leu Ile Val Val Leu Lys Lys
1 5 10 15

Gln Phe Ile Leu Ala Leu Gln Thr Ile Ser Thr Ser Leu Arg Ser Lys
20 25 30

Gln Ile Leu Met Val Leu Ser Ser Thr Ile Ile Ala Asp Ser Thr Phe
35 40 45

Tyr Tyr Xaa
50

<210> 247
<211> 33

<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (33)
<223> Xaa equals stop translation

<400> 247
Met Pro Val Pro Leu Trp Leu Val Leu Trp Phe Cys Phe Leu Leu Tyr
1 5 10 15

Val Ala Ser Arg Arg Thr Phe Gly Leu Ala Asn Tyr Met Pro Leu Pro
20 25 30

Xaa

<210> 248
<211> 49
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (49)
<223> Xaa equals stop translation

<400> 248
Met Leu Ile Cys Arg Leu Val Leu Leu Ala Asp Pro Gly Pro Val Asn
1 5 10 15

Phe Met Val Arg Leu Phe Val Val Ile Val Met Phe Ala Trp Ser Ile
20 25 30

Val Gly Lys Tyr Val Leu Ile Ser Thr Ile Thr Glu Gln Thr Lys Thr
35 40 45

Xaa

<210> 249
<211> 116
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (116)
<223> Xaa equals stop translation

<400> 249
Met Ile Asn Val Tyr Phe Ser Gly Pro Gly Val Leu Thr Pro Leu Asp
1 5 10 15

Asp Gln Gly Ser Pro Cys Pro Pro Ala Pro Phe Ala Ala Leu His Pro

20 25 30

Cys Pro His Pro Ala Gly Ser Gly Val Leu Cys Cys Cys Pro Leu Arg
35 40 45

Leu Cys Arg Pro Cys Arg Ile Leu Phe Thr Gly Pro Leu Leu Leu Thr
50 55 60

Leu His His Leu Leu Cys Glu Thr Ser Pro Ser Gly Ile Gly Val Gly
65 70 75 80

Asn Ile Val Pro Gly Ala Arg Pro Leu Gly Val Asn Pro Val Phe Pro
85 90 95

Ile Ser Ser Cys Asp Leu Gly Gln Val Ala Glu Pro Leu Leu Val Thr
100 105 110

Ile Ser Ser Xaa
115

<210> 250
<211> 75
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (75)
<223> Xaa equals stop translation

<400> 250
Met Thr Asn Val Tyr Ser Leu Asp Gly Ile Leu Val Phe Gly Leu Leu
1 5 10 15

Phe Val Cys Thr Cys Ala Tyr Phe Lys Lys Val Pro Arg Leu Lys Thr
20 25 30

Trp Leu Leu Ser Glu Lys Lys Gly Val Trp Gly Val Phe Tyr Lys Ala
35 40 45

Ala Val Ile Gly Thr Arg Leu His Ala Ala Val Ala Ile Ala Cys Val
50 55 60

Val Met Ala Phe Tyr Val Leu Phe Ile Lys Xaa
65 70 75

<210> 251
<211> 63
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (57)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (63)
<223> Xaa equals stop translation

<400> 251
Met Pro Thr Leu Arg Val Pro Val Leu Ser Val Trp Leu Leu Arg Trp
1 5 10 15

Trp Arg Val Leu Gly Ala Gly Arg Val Leu Pro Asp Ser Leu Ser Leu
20 25 30

Ser Pro Pro Pro Pro Thr Gly Cys Gln Thr Lys Pro Glu Arg Gly Trp
35 40 45

Gly Ser Gln Pro Pro Ser Val Leu Xaa Pro Gln Ala Pro Val Xaa
50 55 60

<210> 252
<211> 73
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (73)
<223> Xaa equals stop translation

<400> 252
Met Val Tyr Tyr Leu Asn Arg Ala Leu Arg Ala Thr Phe Ser Ile Leu
1 5 10 15

Phe Ser Val Val Cys Leu Leu Phe Leu Gly Ser Ile Val Asn Cys Phe
20 25 30

Leu Asn Asp Val Phe Lys Pro Leu Thr Leu Asn Phe Ser Thr Ala Leu
35 40 45

Ser Ala Trp Arg Lys Glu Ser Ser Ala Trp Asn Ser Leu Gly Leu Leu
50 55 60

Pro Pro Thr Asp Glu Tyr Pro Thr Xaa
65 70

<210> 253
<211> 49
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (49)
<223> Xaa equals stop translation

<400> 253
Met Val Val Asn Asp Arg Leu Val Ser Thr Cys Ile Leu Cys Thr Leu

1 5 10 15

His Ile Pro Leu Phe Phe Leu Ile Phe Leu Val Tyr Glu Val His Leu
20 25 30

Val Phe Gln Ile Val Ala Asn Leu Gln Lys Ile Phe Gln Tyr Ile Tyr
35 40 45

Xaa

<210> 254
<211> 41
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (41)
<223> Xaa equals stop translation

<400> 254
Met Ile Ile Leu His Ile Val Val Cys Leu Phe Thr Ile Ser Ile Ile
1 5 10 15

Glu Glu Gln Lys Glu Glu Ile Leu Cys Ser Thr Lys Ser Gln Ala Glu
20 25 30

Lys Thr Val Thr His Ile Glu Gln Xaa
35 40

<210> 255
<211> 54
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (54)
<223> Xaa equals stop translation

<400> 255
Met Thr Leu Ser Val Leu Phe Ala Phe Pro Ile Trp Leu Lys Tyr Leu
1 5 10 15

Asn Leu Asn Ile Phe Phe Leu Ala Leu Lys Ile Phe Trp Val Ile Leu
20 25 30

Ser Phe Cys Thr Ser Cys Thr Ser Trp Tyr Ser Gly Ala Arg Val Ile
35 40 45

Phe Phe Gln Ile Ile Xaa
50

<210> 256

<211> 41
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (41)
<223> Xaa equals stop translation

<400> 256
Met Cys Arg Arg Ile Gln Arg Leu Arg Ala Met Leu His Met Leu Leu
1 5 10 15

Val Ser Met Leu Pro Thr Val Gly Lys Pro Asn Met Tyr Gln Pro Pro
20 25 30

Gln Asn Tyr Asp Ile Leu Leu Gln Xaa
35 40

<210> 257
<211> 42
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (12)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (42)
<223> Xaa equals stop translation

<400> 257
Met Ala Leu Ala Phe Leu His Leu Asn Ile Ser Xaa Ser Gln Ala Leu
1 5 10 15

Thr Leu Cys Lys Glu Leu Glu Lys Pro Lys Leu Glu Lys Asn Lys Gly
20 25 30

Gly Pro Ala Leu Glu Lys Leu Val Val Xaa
35 40

<210> 258
<211> 53
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (53)
<223> Xaa equals stop translation

<400> 258
Met Ser Gly Thr Thr Trp Thr Ala Ile His Leu Thr Ser Asn Leu Phe

1 5 10 15

Gly Ile Leu Ala Leu Pro Gly Asn Gln Ser Ser Gly Ser Asn Ile Glu
20 25 30

Gln Leu Cys Thr Ser Ser Arg Glu Ala Thr Asn Arg Leu Pro Cys Val
35 40 45

Asp Val Gly Ser Xaa
50

<210> 259
<211> 48
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (48)
<223> Xaa equals stop translation

<400> 259
Met Phe Tyr Pro Pro Cys Pro Phe Phe Pro Gln Leu Cys Phe Cys Ile
1 5 10 15

Phe Phe Leu Gly Lys Cys Lys Leu Ser Leu Ser Phe Met Thr Cys Glu
20 25 30

Ile Ser Val Ser Leu Glu Phe Val Arg Arg Arg Gly Asn His Ala Xaa
35 40 45

<210> 260
<211> 53
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (53)
<223> Xaa equals stop translation

<400> 260
Met Asn Ser Trp Ile Leu Asn Met Arg Val Arg Phe Thr Phe Leu Ser
1 5 10 15

Gln Leu Leu Thr Leu Ile Pro Arg Thr Ser His Ser Ala Thr Ser Val
20 25 30

Gly Asn Ser Gln Ile Glu Leu Pro Arg Glu Lys His His Met Thr Tyr
35 40 45

Trp Glu Asn Gly Xaa
50

<210> 261
<211> 55
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (55)
<223> Xaa equals stop translation

<400> 261
Met Phe Ile Val Ile Cys Lys Ile Leu Leu Phe Leu Ile Leu Val Ala
1 5 10 15

Arg Pro Phe Arg Thr His Ser Cys Ile Lys Tyr Phe Ala Leu Phe Lys
20 25 30

Glu Thr His Met Asp Glu Val Arg Met Cys Asn Met Met Ala Ser Gln
35 40 45

Cys Ser Ser Leu Tyr Leu Xaa
50 55

<210> 262
<211> 38
<212> PRT
<213> Homo sapiens

<400> 262
Met Lys Asn Met Asn Ser Arg Tyr Tyr Leu Arg Ala Ile Phe Cys Leu
1 5 10 15

Tyr Thr Leu Ala Cys Ile Leu Phe Leu Gln Ile Ile Leu Lys Ala Arg
20 25 30

Cys Gly Gly Ser Arg Leu
35

<210> 263
<211> 24
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (24)
<223> Xaa equals stop translation

<400> 263
Met Pro Pro Leu Phe Leu Gly Ser Phe Leu Val Leu Trp Leu Gly Gly
1 5 10 15

Val Val Leu Cys Thr Gly Gly Xaa
20

<210> 264
<211> 47
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (11)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (47)
<223> Xaa equals stop translation

<400> 264
Met Val Cys Ala Leu Gly Val Tyr Val Cys Xaa Ser Ala Pro Thr Ala
1 5 10 15

Ala Val Pro Lys Pro Ala Lys Gly Thr Ile Cys Leu Lys Met Leu Ser
20 25 30

Gly Ala Asn Cys Ala Cys Gln Gly Gln Val Thr Arg Gln His Xaa
35 40 45

<210> 265
<211> 115
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (13)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (115)
<223> Xaa equals stop translation

<400> 265
Met Ala Gly Pro Arg Ala Ser Thr Gly Pro Arg Pro Xaa Cys Leu Val
1 5 10 15

Leu Phe Leu Phe Asn Phe Ile Phe Cys Phe Met Ser Val Cys Pro Pro
20 25 30

Thr Pro Thr Pro Phe Ser Val Lys Trp Gly Ala Leu Gly Glu Ser Leu
35 40 45

Leu Pro Pro Ser Leu Ser Gln Asp Leu Pro Pro Arg His Gln Pro Ser
50 55 60

Leu Trp Thr Arg Gln Arg Ala Asp Arg Val Gly Arg Gly Leu Arg Val
65 70 75 80

```
Ala Arg Ala Ser Pro Pro Ala Asn Gly Pro Leu Leu Arg Pro Pro Val
                85                  90                  95

Ser Pro Cys Pro Phe Leu Lys Gln Asn Ala Leu Val Cys Lys Pro Leu
            100                 105                 110

Asp Ala Xaa
        115
```

<210> 266
<211> 248
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (166)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (248)
<223> Xaa equals stop translation

<400> 266

```
Met His Leu Ala Arg Leu Val Gly Ser Cys Ser Leu Leu Leu Leu Leu
  1               5                  10                  15

Gly Ala Leu Ser Gly Trp Ala Ala Ser Asp Asp Pro Ile Glu Lys Val
             20                  25                  30

Ile Glu Gly Ile Asn Arg Gly Leu Ser Asn Ala Glu Arg Glu Val Gly
         35                  40                  45

Lys Ala Leu Asp Gly Ile Asn Ser Gly Ile Thr His Ala Gly Arg Glu
     50                  55                  60

Val Glu Lys Val Phe Asn Gly Leu Ser Asn Met Gly Ser His Thr Gly
 65                  70                  75                  80

Lys Glu Leu Asp Lys Gly Val Gln Gly Leu Asn His Gly Met Asp Lys
                 85                  90                  95

Val Ala His Glu Ile Asn His Gly Ile Gly Gln Ala Gly Lys Glu Ala
            100                 105                 110

Glu Lys Leu Gly His Gly Val Asn Asn Ala Ala Gly Gln Ala Gly Lys
        115                 120                 125

Glu Ala Asp Lys Ala Val Gln Gly Phe His Thr Gly Val His Gln Ala
    130                 135                 140

Gly Lys Glu Ala Glu Lys Leu Gly Gln Gly Val Asn His Ala Ala Asp
145                 150                 155                 160

Gln Ala Gly Lys Glu Xaa Glu Lys Leu Gly Pro Ser Ala His His Ala
```



```
                165                 170                 175

Ala Gly Gln Ala Gly Lys Glu Leu Gln Asn Ala His Asn Gly Val Asn
            180                 185                 190

Gln Ala Ser Lys Glu Ala Asn Gln Leu Leu Asn Gly Asn His Gln Ser
        195                 200                 205

Gly Ser Ser Ser His Gln Gly Gly Ala Thr Thr Thr Pro Leu Ala Ser
    210                 215                 220

Gly Ala Ser Val Asn Thr Pro Phe Ile Asn Leu Pro Ala Leu Trp Arg
225                 230                 235                 240

Ser Val Ala Asn Ile Met Pro Xaa
                245
```

<210> 267
<211> 178
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (155)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (178)
<223> Xaa equals stop translation

<400> 267

```
Met Leu Phe Leu Phe Leu Tyr Cys Leu Leu Val Val Leu Pro Phe Lys
  1               5                  10                  15

Leu Thr Pro Lys His Ser Ala Glu Val Leu Leu Ser Ile His Lys Ser
             20                  25                  30

Lys Lys Tyr Leu Cys Lys Val Lys Ala Ala Cys Lys Ile Gln Ala Trp
         35                  40                  45

Tyr Arg Cys Trp Arg Ala His Lys Glu Tyr Leu Ala Ile Leu Lys Ala
     50                  55                  60

Val Lys Ile Ile Gln Gly Cys Phe Tyr Thr Lys Leu Glu Arg Thr Arg
 65                  70                  75                  80

Phe Leu Asn Val Arg Ala Ser Ala Ile Ile Ile Gln Arg Lys Trp Arg
                 85                  90                  95

Ala Ile Leu Pro Ala Lys Ile Ala His Glu His Phe Leu Met Ile Lys
            100                 105                 110

Arg His Arg Ala Ala Cys Leu Ile Gln Ala His Tyr Arg Gly Tyr Lys
        115                 120                 125
```

Gly Arg Gln Val Phe Leu Arg Gln Lys Ser Ala Ala Leu Ile Ile Gln
130 135 140

Lys Tyr Ile Arg Ala Arg Glu Ala Gly Lys Xaa Glu Arg Ile Lys Tyr
145 150 155 160

Ile Glu Phe Lys Asn Leu Gln Leu Ser Tyr Lys His Trp Cys Val Val
165 170 175

Gly Xaa

<210> 268
<211> 79
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (79)
<223> Xaa equals stop translation

<400> 268
Met Arg Pro Leu Leu Gly Leu Leu Leu Val Phe Ala Gly Cys Thr Phe
1 5 10 15

Ala Leu Tyr Leu Leu Ser Thr Arg Leu Pro Arg Gly Arg Arg Leu Gly
20 25 30

Ser Thr Glu Glu Ala Gly Gly Arg Ser Leu Trp Phe Pro Ser Asp Leu
35 40 45

Ala Glu Leu Arg Glu Leu Ser Glu Val Leu Arg Glu Tyr Arg Lys Glu
50 55 60

His Gln Ala Tyr Val Phe Leu Leu Phe Cys Gly Ala Tyr Leu Xaa
65 70 75

<210> 269
<211> 81
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (81)
<223> Xaa equals stop translation

<400> 269
Met Lys Leu Ser Gly Met Phe Leu Leu Leu Ser Leu Ala Leu Phe Cys
1 5 10 15

Phe Leu Thr Gly Val Phe Ser Gln Gly Gly Gln Val Asp Cys Gly Glu
20 25 30

Phe Gln Asp Thr Lys Val Tyr Cys Thr Arg Glu Ser Asn Pro His Cys

35 40 45

Gly Ser Asp Gly Gln Thr Tyr Gly Asn Lys Cys Ala Phe Cys Lys Ala
50 55 60

Ile Val Lys Ser Gly Gly Lys Ile Ser Leu Lys His Pro Gly Lys Cys
65 70 75 80

Xaa

<210> 270
<211> 69
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (69)
<223> Xaa equals stop translation

<400> 270
Met Asp Ala Ala Met Pro Val Cys Pro Cys Leu Ile Cys Val Cys Phe
1 5 10 15

Val Leu Arg Leu Gln Ser Gly Val Ala Gly Thr Glu Thr Glu Arg Pro
20 25 30

Pro His Gly Ala Ala Ser Leu His Gln Asp Arg Gly Ala Thr Leu Arg
35 40 45

Leu Cys Phe Phe Pro Ser Gly Val Gly Phe Leu Leu Phe Leu Ser Ile
50 55 60

Leu Pro Trp Ser Xaa
65

<210> 271
<211> 131
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (131)
<223> Xaa equals stop translation

<400> 271
Met Asn Phe Arg Gln Arg Met Gly Trp Ile Gly Val Gly Leu Tyr Leu
1 5 10 15

Leu Ala Ser Ala Ala Ala Phe Tyr Tyr Val Phe Glu Ile Ser Glu Thr
20 25 30

Tyr Asn Arg Leu Ala Leu Glu His Ile Gln Gln His Pro Glu Glu Pro
35 40 45

```
Leu Glu Gly Thr Thr Trp Thr His Ser Leu Lys Ala Gln Leu Leu Ser
     50                  55                  60

Leu Pro Phe Trp Val Trp Thr Val Ile Phe Leu Val Pro Tyr Leu Gln
 65                  70                  75                  80

Met Phe Leu Phe Leu Tyr Ser Cys Thr Arg Ala Asp Pro Lys Thr Val
                 85                  90                  95

Gly Tyr Cys Ile Ile Pro Ile Cys Leu Ala Val Ile Cys Asn Arg His
            100                 105                 110

Gln Ala Phe Val Lys Ala Ser Asn Gln Ile Ser Arg Leu Gln Leu Ile
        115                 120                 125

Asp Thr Xaa
    130


<210> 272
<211> 85
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (65)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (85)
<223> Xaa equals stop translation

<400> 272
Met Trp Val Phe Phe Leu Pro Phe Phe Ser Ile Leu Phe Lys Ile Cys
  1               5                  10                  15

Trp Cys Ile Ser Leu Ser Gln Thr Lys Glu Lys Gln Ser Ser Asn Leu
             20                  25                  30

Met Phe Tyr Phe Phe Cys Ile Cys Thr Tyr Glu Arg Arg Arg Lys Lys
         35                  40                  45

Glu Met Arg Arg Gly Glu Lys Lys Arg Ser Phe Cys Leu Ile Gly Leu
     50                  55                  60

Xaa Gln His Met Ile Ala Val Gln Ala Trp Phe His Glu Gln His Gln
 65                  70                  75                  80

Ile Gln Ile Ser Xaa
                 85


<210> 273
<211> 79
<212> PRT
```



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<213> Homo sapiens

<220>
<221> SITE
<222> (61)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (79)
<223> Xaa equals stop translation

<400> 273
Met Gln Trp Pro Phe Leu Cys Val Leu Pro Leu Leu Pro Gln Val Trp
  1               5                  10                  15

Arg Ala Gly Ser Leu Leu Arg Ala Leu Glu Leu Tyr Ser Val Leu Leu
             20                  25                  30

Ser His Phe Leu Trp Glu Met Trp Thr Met Ser Leu Lys Glu Pro Glu
         35                  40                  45

Leu Leu Leu Ser Thr Lys Ser Leu Thr Val Trp Arg Xaa Arg Glu Pro
     50                  55                  60

Leu Ser Glu Ile Gly Gly Cys Arg Leu Asn Asn Glu Gly Thr Xaa
 65                  70                  75


<210> 274
<211> 54
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (54)
<223> Xaa equals stop translation

<400> 274
Met Phe Cys Phe Asn Trp Leu Leu Cys Phe Leu Phe Pro Arg Phe Pro
  1               5                  10                  15

Ile Leu Val Cys Arg Lys His Gln Phe Cys Val Tyr Leu Leu Leu Val
             20                  25                  30

Leu Lys Leu Arg Thr Leu Tyr Ala Glu Leu Ile Asp Leu His Leu Cys
         35                  40                  45

Ala Ser Ile Leu Gly Xaa
     50


<210> 275
<211> 155
<212> PRT
<213> Homo sapiens
```

<220>
<221> SITE
<222> (150)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (155)
<223> Xaa equals stop translation

<400> 275
Met Ala Arg His Gly Leu Pro Leu Leu Pro Leu Leu Ser Leu Leu Val
1 5 10 15

Gly Ala Trp Leu Lys Leu Gly Asn Gly Gln Ala Thr Ser Met Val Gln
20 25 30

Leu Gln Gly Gly Arg Phe Leu Met Gly Thr Asn Ser Pro Asp Ser Arg
35 40 45

Asp Gly Glu Gly Pro Val Arg Glu Ala Thr Val Lys Pro Phe Ala Ile
50 55 60

Asp Ile Phe Pro Val Thr Asn Lys Asp Phe Arg Asp Phe Val Arg Glu
65 70 75 80

Lys Lys Tyr Arg Thr Glu Ala Glu Met Phe Gly Trp Ser Phe Val Phe
85 90 95

Glu Asp Phe Val Ser Asp Glu Leu Arg Asn Lys Ala Thr Gln Pro Met
100 105 110

Lys Ser Val Leu Trp Trp Leu Pro Val Glu Lys Ala Phe Trp Arg Gln
115 120 125

Pro Ala Gly Pro Gly Ser Gly Ile Arg Glu Arg Leu Glu His Pro Val
130 135 140

Leu His Val Ser Trp Xaa Asp Ala Arg Ala Xaa
145 150 155

<210> 276
<211> 129
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (68)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (98)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE
<222> (103)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (104)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (112)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (114)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (124)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (129)
<223> Xaa equals stop translation

<400> 276
Met Ala Tyr Arg His Phe Trp Met Leu Val Leu Phe Val Ile Phe Asn
1 5 10 15

Ser Leu Gln Gly Leu Tyr Val Phe Met Val Tyr Phe Ile Leu His Asn
20 25 30

Gln Met Cys Cys Pro Met Lys Ala Ser Tyr Thr Val Glu Met Asn Gly
35 40 45

His Pro Gly Pro Ser Thr Ala Phe Phe Thr Pro Gly Ser Gly Met Pro
50 55 60

Pro Ala Gly Xaa Glu Ile Ser Lys Ser Thr Gln Asn Leu Asn Arg Trp
65 70 75 80

Tyr Gly Gly Arg Cys His Leu Thr Gly Arg Glu His Pro Ser Lys Gln
85 90 95

Gly Xaa Gln Gly Gln Pro Xaa Xaa Lys Ala Lys Ser Thr Lys Trp Xaa
100 105 110

His Xaa Pro Val Leu Trp Arg Ile Trp Pro Gly Xaa Thr Asp Ser Arg
115 120 125

Xaa

<210> 277
<211> 84
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (84)
<223> Xaa equals stop translation

<400> 277
Met Ala Ser Pro Gly Trp His Leu Ser Cys Arg Pro Thr Gly Leu Val
1 5 10 15

Ser Ile Phe Leu Leu Cys Ala Pro Ala Tyr Leu His Ser Phe Val Met
20 25 30

Thr Ser Ile Thr Leu Ile Ser Thr Lys Ile Cys Ser Pro Thr Lys Leu
35 40 45

Arg His Arg Thr His Phe Leu Tyr Gly Ser Ile Met Glu Leu Tyr Pro
50 55 60

Thr Leu Thr Phe Pro Met Thr Thr Asp Val Glu Asn Leu Asn Leu Asp
65 70 75 80

Ser Ser Arg Xaa

<210> 278
<211> 86
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (86)
<223> Xaa equals stop translation

<400> 278
Met Gly Cys Arg Gly Asn Lys Leu Phe Val Leu Ser Tyr Cys Thr Cys
1 5 10 15

Leu Thr Trp Leu Leu Gly Thr Lys Ser Gln Lys Asn Pro Phe Gln Val
20 25 30

Cys Met Ser Gly Gly Trp Ala Val Ser Arg Leu Glu Thr Gly Phe Gln
35 40 45

Ala Leu His Asp Gly Arg Ala Ser Ser Pro Leu Ser Ala Ala Cys Val
50 55 60

Leu Asp Arg Thr Val Ala Arg Arg Trp Lys Pro Pro Ser Val Pro Leu
65 70 75 80

Ala His His Thr Lys Xaa
85

<210> 279
<211> 96
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (96)
<223> Xaa equals stop translation

<400> 279
Met Pro Trp Leu Thr Ile Leu Arg Phe Leu Gln Ala Ser Gly His Val
1 5 10 15

Arg Ala Gln Asp Leu Ala Leu Leu Gly Asp Thr Ser Val Cys Ile Arg
20 25 30

Cys Gly Cys Gly Gly Cys Ser Leu Ser Ile Ala Asn Tyr Glu Trp Val
35 40 45

Pro Leu Arg Arg Lys Asp Cys Lys Arg Tyr Glu Thr Ser Glu Lys Thr
50 55 60

Ser Cys Leu Leu Leu Pro Ser Ala Cys Ser Arg Gln Asn Ala Val Gly
65 70 75 80

Phe Ser Arg Leu Pro Val Pro Lys Leu Ser Cys Leu Leu His Gly Xaa
85 90 95

<210> 280
<211> 98
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (70)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (98)
<223> Xaa equals stop translation

<400> 280
Met Ile Leu Leu Phe Leu Leu Ser Leu Ser Leu Ser Leu Leu Ser Leu
1 5 10 15

Ser Leu Ser Phe Ser Pro Leu Asn Cys Leu Phe Ser Phe Trp Gly Ser
20 25 30

Pro Pro Thr Arg Cys Ser Trp Cys Arg Leu Gly Ser Gln Gly Glu Ala

```
        35                  40                  45

Trp Trp Pro Gly Leu Gly Arg Gly Thr Leu Ser Leu Ala Lys Ala Glu
     50                  55                  60

Ser Glu Ile Val Val Xaa Leu Cys Lys Ser Tyr Phe Gln Tyr Phe Leu
 65                  70                  75                  80

Ala Ala Ser Glu Val Ser Leu Thr Pro Cys Arg Ala Leu Leu Leu Leu
                 85                  90                  95

Ser Xaa
```

<210> 281
<211> 55
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (55)
<223> Xaa equals stop translation

<400> 281

```
Met Ser Val Trp Pro Arg Ser Thr Leu Leu Phe Cys Leu Leu Ser Leu
  1               5                  10                  15

Ser Thr Gly Leu Phe Leu Asp Lys Leu Gly Ile Ile Ile Pro Ile Leu
             20                  25                  30

Leu Cys Gly Trp Lys Leu Asn Val Ile Met Met Cys Val Arg Cys Leu
         35                  40                  45

His Ser Ala Trp Arg Tyr Xaa
     50                  55
```

<210> 282
<211> 72
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (72)
<223> Xaa equals stop translation

<400> 282

```
Met Arg Ile His Phe Lys Ile Leu Val Leu Val Ile Tyr Phe Ile Leu
  1               5                  10                  15

Leu Gly Ser Phe Ser Asp Arg Cys Ser Leu Leu Asp Cys Lys Ser Arg
             20                  25                  30

Ile Gln Arg Ile Phe Ile Cys Asn Ile Leu Asn Leu Ser Leu Val Ser
         35                  40                  45
```



```
Cys His Leu Cys Arg Tyr Ser Phe Asp Cys Leu Thr Arg Gly Lys Cys
     50                  55                  60

Phe Pro Leu Ser Phe Pro Ala Xaa
 65                  70
```

<210> 283
<211> 44
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (44)
<223> Xaa equals stop translation

<400> 283

```
Met Tyr Ala Ala Ala Leu Ser Thr Ala Pro Ser Leu Phe Phe Leu His
  1               5                  10                  15

Leu Cys Leu Leu Lys Thr Leu Ile Leu Phe Ser Leu Ser Ser Ile Pro
             20                  25                  30

Leu Pro Pro Leu Leu Tyr Ser Tyr Asp Leu His Xaa
         35                  40
```

<210> 284
<211> 56
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (56)
<223> Xaa equals stop translation

<400> 284

```
Met Leu Pro Ser Asn Trp Ser Gly Thr Trp Ala Leu Ile Gln Leu Ser
  1               5                  10                  15

Ile Pro Phe Thr Leu Ala Phe His Gln Pro Asn Lys Asn Gln Leu Thr
             20                  25                  30

Gln Lys Lys Arg Lys Ala Pro Gln Gly Ser Phe Asp Pro Asp Ile Tyr
         35                  40                  45

Ile Asp Ala Ile Gly Val Pro Xaa
     50                  55
```

<210> 285
<211> 49
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (49)
<223> Xaa equals stop translation

<400> 285
Met Ser Thr Leu Arg Arg Met Ala Leu Leu Tyr Ile Glu Thr Pro Leu
1 5 10 15

Leu Arg Ala Leu Met Val Gln Gly Pro Arg Leu Val Ser Val Arg Ala
20 25 30

Ala Met His Gly Lys Cys Gly Gly Arg Ala Leu Trp Ala Leu Trp Gln
35 40 45

Xaa

<210> 286
<211> 42
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (42)
<223> Xaa equals stop translation

<400> 286
Met Val Cys Val Arg Cys Val Trp Tyr Val Trp His Val Phe Gly Val
1 5 10 15

Tyr Gly Asn Ile Leu Trp Ile Arg Thr Cys Gly Leu Phe Lys Asp Leu
20 25 30

Ser Phe Cys Ala Leu Lys Ser Glu Met Xaa
35 40

<210> 287
<211> 49
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (49)
<223> Xaa equals stop translation

<400> 287
Met Arg His Val Ala Ile Val Thr Met Ile Val Val Leu Ser Pro Pro
1 5 10 15

Val Leu Ala Ser Ser Leu Lys Pro Pro Leu Phe Ile Asp Thr Tyr Phe
20 25 30

Met Phe Gly Lys Arg Cys Ser Arg Trp Asp Thr Pro Ala Cys Ser Lys

35 40 45

Xaa

<210> 288
<211> 110
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (110)
<223> Xaa equals stop translation

<400> 288
Met Trp Ala Glu Leu Lys Leu Leu Ser Trp Gly Arg Ala Ala Ile Ala
1 5 10 15

Val Trp Val Cys Leu Arg Arg Val Val Arg Gly Gly His Ser Pro Pro
20 25 30

Ala Gly Gln Gly Gly Gln Gly Val Lys Val Gln Trp Glu Gly Val Gln
35 40 45

Gly Ser Gly Ser Gly Gln Pro Glu Asp Met Arg Trp Glu Lys Leu His
50 55 60

Val Arg Ile Leu Met Gln Gly Met His Gly Ala Pro Gln Asp Asp Ile
65 70 75 80

Arg Ser Val His Gly Ser Thr Ala Phe Pro Asp Cys Leu His Leu Pro
85 90 95

Cys Arg Pro Thr Cys Pro Gly Val Ser Phe Gly Ser Gly Xaa
100 105 110

<210> 289
<211> 64
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (64)
<223> Xaa equals stop translation

<400> 289
Met Leu Leu Val Ser Cys Phe Met Ser Ile Tyr Phe Leu Ser Pro Leu
1 5 10 15

Leu Leu Pro Leu His Gly Ser Pro His Pro His Ser Tyr Leu Cys Phe
20 25 30

Ala Val Cys Arg Thr Ser Trp Ser Leu Ser Glu Lys Thr Cys Asn Phe
35 40 45

```
Pro Asn Glu Met Leu Gln Leu Pro Ile Phe Leu Lys Ser Ile Tyr Xaa
     50                  55                  60
```

<210> 290
<211> 42
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (42)
<223> Xaa equals stop translation

<400> 290
```
Met Gly Leu Leu Leu Leu Leu Leu Leu Gly Cys Trp Thr His Ile Phe
  1               5                  10                  15

Phe Thr Asn Gly Met Ile Tyr Trp Tyr Leu Glu Gly His Pro Ile Leu
             20                  25                  30

Asn Glu Ile Leu Phe Ile Leu His Phe Xaa
         35                  40
```

<210> 291
<211> 43
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (43)
<223> Xaa equals stop translation

<400> 291
```
Met Ile Asn Cys Val Cys Val His Ala Cys Val Arg Ala Cys Gly Leu
  1               5                  10                  15

Leu His Ser Leu Val Leu Leu Leu Ser Leu Ser Leu Ser Ser Ala Leu
             20                  25                  30

Phe Ile Pro Trp Asp Thr Glu Ile Phe Lys Xaa
         35                  40
```

<210> 292
<211> 45
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (45)

<223> Xaa equals stop translation

<400> 292
```
Met Leu Phe Phe Cys Leu Leu Met Lys Met Leu Gly Pro Ser Arg Leu
  1               5                  10                  15

Pro Phe Leu Ala Leu Thr Leu Cys Arg Phe Ile Leu Tyr Phe Gln Phe
             20                  25                  30

Cys Tyr Leu Ile Ser Asp Ser Ser Pro Asp His Ser Xaa
         35                  40                  45
```

<210> 293
<211> 57
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (57)
<223> Xaa equals stop translation

<400> 293
```
Met Cys Phe Thr Gln Phe Ser Arg Ile Phe Phe Leu Thr Ser Ser Leu
  1               5                  10                  15

Thr Leu Ala Ala Cys Ala Asn His Ile Leu Ala Ala Tyr Ser Ser Ser
             20                  25                  30

Leu Ala Asp Arg Cys Val Gly Glu Lys Ser Leu Ile Val Ile Val Pro
         35                  40                  45

Glu Arg Ser Phe Gln Thr His Phe Xaa
     50                  55
```

<210> 294
<211> 75
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (75)
<223> Xaa equals stop translation

<400> 294
```
Met Met Tyr Val Gln Ser Ala Ile Met Ser Leu Gln His Leu Leu Val
  1               5                  10                  15

Leu His Arg Val Ile Ile Ile Ser Met His Phe Ala Phe Gly Asn Gly
             20                  25                  30

Cys Thr Phe Lys Ile Leu Val Gln Cys Ala Ile Arg Lys Tyr Thr Ser
         35                  40                  45

Lys Met Ile Ser Arg Ile Ile Gln Met Tyr Leu Thr Thr Met Asp Leu
```

50 55 60

Phe His Pro Met Lys Leu Gln Arg Lys Leu Xaa
65 70 75

<210> 295
<211> 51
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (51)
<223> Xaa equals stop translation

<400> 295
Met Ile Ile Pro Lys Phe Tyr Leu Phe Lys Leu Leu Leu Leu Leu Gln
1 5 10 15

Lys Ile Thr His Phe Ile Cys Gly Lys Thr Leu Asn Asn Leu Asn Phe
20 25 30

Arg Cys Glu Ser Tyr Phe Leu Phe Leu Tyr Leu Tyr Cys Ala Tyr Ile
35 40 45

Leu Tyr Xaa
50

<210> 296
<211> 45
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (45)
<223> Xaa equals stop translation

<400> 296
Met Thr Gln Glu Ile Leu Val Val Phe Ser Ile Gln Val Leu Ser Ser
1 5 10 15

Leu Arg Leu Leu Gly Leu Trp Phe Phe Met Glu Asn Arg Leu Cys Ser
20 25 30

Gly Ile Val Glu Gln Arg Arg Leu Leu His Leu Asn Xaa
35 40 45

<210> 297
<211> 48
<212> PRT
<213> Homo sapiens

<220>
<221> SITE

<222> (48)
<223> Xaa equals stop translation

<400> 297
Met Pro Thr Leu Gly Asp Ala Leu Ile Leu Tyr Leu His Leu Val Leu
1 5 10 15

Gly Val Ala Gly Val Leu Gln Pro Pro Gly Pro Arg Pro Ser Gln Ala
20 25 30

Leu Gly Pro Thr Gly Asp Arg Ala Pro Gly Lys Trp Asn Arg Ser Xaa
35 40 45

<210> 298
<211> 55
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (55)
<223> Xaa equals stop translation

<400> 298
Met Ala Trp Cys Leu Leu Ser Val Phe Phe Leu Arg Ala Leu Cys Ala
1 5 10 15

His Ser Ser Thr Ala Tyr Lys Cys Val Leu Cys Ser Pro Arg Ser Pro
20 25 30

Trp Leu Val Glu Ala Asn Phe Trp Leu Asp Phe Tyr Gly Lys Ser Tyr
35 40 45

Phe Met Ser Pro Lys His Xaa
50 55

<210> 299
<211> 30
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (30)
<223> Xaa equals stop translation

<400> 299
Met Gln Met Thr Val Val Trp Tyr Val Ile Thr Ala Ile Ile Trp Trp
1 5 10 15

Arg Met Ser Met Cys Glu Ala Leu Ser Gln Asn Cys Phe Xaa
20 25 30

<210> 300
<211> 73
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (73)
<223> Xaa equals stop translation

<400> 300
Met Pro Leu Gly Val Val Pro Arg Ala Val Trp Ser Thr Leu Ala Trp
1 5 10 15

Val Cys Ile Ile Leu Gln Thr Leu Lys Thr Ser Leu Phe Cys Gln Thr
20 25 30

Thr Phe Cys Gly Glu Pro Glu Asp Ser Gly Phe Phe Glu Gly Ile Leu
35 40 45

Asp Val Cys Val Leu Val Lys Glu Ala Val Ile Arg Leu Asn His Asn
50 55 60

Pro Gln Asp Leu Leu Asp Ser Asp Xaa
65 70

<210> 301
<211> 37
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (37)
<223> Xaa equals stop translation

<400> 301
Met Leu Arg Leu Glu Val Leu Leu Leu Phe Phe Ser Lys Val Thr Asp
1 5 10 15

Gln Ile Ile Thr Gln Ile Ile Gln Glu Asn Arg Ser Glu Ile Lys Asn
20 25 30

Asn Ile Ile Phe Xaa
35

<210> 302
<211> 49
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (49)
<223> Xaa equals stop translation

<400> 302
Met Arg Pro Val Leu Arg Arg Thr Phe Leu Leu Thr Leu Phe Ser Val
1 5 10 15

Ile Ala Leu Thr Lys Ile Lys His Asp Phe Phe Ile Met Cys Ser His
20 25 30

Met Gln Cys Ile Pro Arg Val Phe Leu Lys His Glu Phe Asn Asn Ile
35 40 45

Xaa

<210> 303
<211> 42
<212> PRT
<213> Homo sapiens

<400> 303
Met Phe Tyr Thr Thr Leu Cys Lys Met Phe Gln Tyr Leu His Ile Leu
1 5 10 15

Ser Leu Ser Phe Cys Phe Ala Leu Ile Trp Trp Ser Glu Ser Phe Leu
20 25 30

Trp Leu Ser Asn Leu Val Arg Leu Arg His
35 40

<210> 304
<211> 54
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (54)
<223> Xaa equals stop translation

<400> 304
Met Ile Leu Leu Ile Ser Gln Cys Pro Leu Ser Ile Phe Ala Ala Pro
1 5 10 15

Phe Ala Leu Pro Pro Lys Gly His Cys Gly Ser Phe Ser Asp Phe His
20 25 30

Ser Gln Val Thr Leu His Lys Asn Ser Lys Leu Ile Phe Arg Ser His
35 40 45

Lys Ser Ile Leu Leu Xaa
50

<210> 305
<211> 76
<212> PRT

<213> Homo sapiens

<220>
<221> SITE
<222> (76)
<223> Xaa equals stop translation

<400> 305
Met Leu Ala Ala Glu Leu Ile Cys Cys Pro Ser Leu His Ile Phe Phe
1 5 10 15

Phe Ala Ala Phe Ser Leu Trp Gln Cys Thr Val Leu Thr Met Pro Phe
20 25 30

Lys Asn Val Pro Tyr Cys Ile Ser Ile Leu Arg Arg Asp Arg Thr Lys
35 40 45

Lys Tyr Ile Ala Gln Ile Ile Phe Tyr Phe Ile Asp Asn Asp Lys Glu
50 55 60

Tyr Phe Leu Asn Pro Ile Lys Ile Asp Phe Asn Xaa
65 70 75

<210> 306
<211> 63
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (63)
<223> Xaa equals stop translation

<400> 306
Met Phe Phe Arg Met Gln Val Cys Glu His His Gly Phe Trp Val Ile
1 5 10 15

Leu Leu Leu Leu Ser Leu Lys Met Glu Ile Pro Leu Ala Ala Tyr Pro
20 25 30

Thr Ala Glu Tyr Ser Ser Ile Gly Ser Gly Phe Thr Pro Leu His Pro
35 40 45

Ser Arg Thr Phe Thr Gln Ala Ser Pro Leu Pro Ser Ile Phe Xaa
50 55 60

<210> 307
<211> 50
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (50)
<223> Xaa equals stop translation

<400> 307
Met Asn Val Phe Val Gly Pro Leu Ser Val Ala Ile Val Ile Phe Cys
1 5 10 15

Trp Ile Thr Met Tyr Trp Val Ser Ile Val Met Gly Gln Gly Arg Gly
20 25 30

Gln Tyr Thr Trp Arg Thr Ile Leu Ser Thr Ser Thr Pro Ser Val Cys
35 40 45

Ser Xaa
50

<210> 308
<211> 103
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (103)
<223> Xaa equals stop translation

<400> 308
Met Glu His Trp Ile Pro Pro Glu Val Pro Leu Ala Gly Leu Arg Arg
1 5 10 15

Leu Leu Leu Asp Arg Leu Val Phe Ala Pro Ala Phe Leu Met Leu Phe
20 25 30

Phe Leu Ile Met Asn Phe Leu Glu Gly Lys Asp Ala Ser Ala Phe Ala
35 40 45

Ala Lys Met Arg Gly Gly Phe Trp Pro Ala Leu Arg Met Asn Trp Arg
50 55 60

Val Trp Thr Pro Leu Gln Phe Ile Asn Ile Asn Tyr Val Pro Leu Lys
65 70 75 80

Phe Arg Val Leu Phe Ala Asn Leu Ala Ala Leu Phe Trp Tyr Ala Tyr
85 90 95

Leu Ala Ser Leu Gly Lys Xaa
100

<210> 309
<211> 45
<212> PRT
<213> Homo sapiens

<400> 309
Met Arg Phe Ile Ser Gln Gln Ser Cys Glu Cys Val Arg Pro Cys Met
1 5 10 15

Asp Val Tyr Val Cys Val Tyr Ile Ser Ile His Val Tyr Met Asp Ala
20 25 30

His Val Tyr Leu Cys Arg Ile Cys Lys Thr Asn Met Arg
35 40 45

<210> 310
<211> 53
<212> PRT
<213> Homo sapiens

<400> 310
Arg Ile Leu Arg Trp Val Asn Cys Met Ala Cys Asp Leu Tyr Leu Asn
1 5 10 15

Lys Ala Val Ser Val Cys Ala His Val Trp Met Cys Met Cys Val Tyr
20 25 30

Ile Ser Leu Tyr Met Tyr Thr Trp Met Pro Met Cys Ile Tyr Val Glu
35 40 45

Tyr Val Lys Gln Thr
50

<210> 311
<211> 59
<212> PRT
<213> Homo sapiens

<400> 311
Asn Pro Glu Asn Gln Leu Glu Ile Ser Phe Pro Pro Arg Arg Gln Lys
1 5 10 15

Met Lys Leu Thr Leu Asp Leu Gln Val Ser Gln Ser Ser Leu Val His
20 25 30

Ser Leu Leu Ser Ser Asp Phe Phe Ser Val Ser Lys Glu Gly Cys Leu
35 40 45

Trp Lys Pro Ile Leu Leu Pro Ser His Phe Leu
50 55

<210> 312
<211> 47
<212> PRT
<213> Homo sapiens

<400> 312
Leu Gln Thr Gln Ile Ser Asn Tyr Leu Met Phe Val Leu His Ile Leu
1 5 10 15

His Arg Tyr Thr Trp Ala Ser Met Tyr Thr Cys Ile Glu Ile Tyr Thr
20 25 30

His Thr Tyr Thr Ser Ile His Gly Arg Thr His Ser Gln Leu Cys
35 40 45

<210> 313
<211> 45
<212> PRT
<213> Homo sapiens

<400> 313
Ile His Met Gly Ile His Val Tyr Met Tyr Arg Asp Ile Tyr Thr His
1 5 10 15

Ile His Ile His Thr Trp Ala His Thr Leu Thr Ala Leu Leu Arg Tyr
20 25 30

Lys Ser His Ala Ile Gln Leu Thr His Leu Asn Ile Arg
35 40 45

<210> 314
<211> 41
<212> PRT
<213> Homo sapiens

<400> 314
Met Lys Trp Ile Phe Thr Val Leu Ile Leu Thr Ser Cys Phe Phe Thr
1 5 10 15

Ala Gly Ile Cys Glu Asp Gly Ile Cys Ser Arg Ile Gln Leu Arg Asp
20 25 30

Lys Ile Val Gln Ser Ala Phe Arg Gln
35 40

<210> 315
<211> 81
<212> PRT
<213> Homo sapiens

<400> 315
Lys Pro Cys Cys Pro Ser Val Ser Asn Arg Ser Ser Val Gln Met His
1 5 10 15

Gln Leu Pro Ile Gln Phe Leu Gly Gln Phe Glu Ala His Cys Ile Gly
20 25 30

Phe Cys Arg Ser Phe Leu Glu Thr Phe Tyr Thr His Asp Pro Arg Ala
35 40 45

Met His Ser Phe Leu Ser Ser Ile Ser Ser Pro Ser Leu Pro Phe Gly
50 55 60

Phe Ser Arg Met Thr Ser Gln Ile Asn His Leu His Pro Ser Pro Leu
65 70 75 80

Cys

<210> 316
<211> 21
<212> PRT
<213> Homo sapiens

<400> 316
Ser Val Phe Lys Ile Asn Leu Lys Ser Phe Lys Gln His Glu Pro Trp
1 5 10 15

Trp Pro Asn Arg Ser
20

<210> 317
<211> 135
<212> PRT
<213> Homo sapiens

<400> 317
Gly Thr Arg Ser Phe Ser Val Pro Ser Tyr Leu Arg Leu Thr Gly Ser
1 5 10 15

Leu Met Cys Tyr Leu Leu Leu Leu Leu Ile Gln Thr Ala Glu Leu Leu
20 25 30

Ile His Pro Gln Gly Leu Gln Ala Val Ser Asn Gly Glu Ser Ala Leu
35 40 45

Lys Gly Thr Arg Pro Thr Phe Ser Ser Pro Phe Ile Leu Val Thr Glu
50 55 60

Gly Arg Lys Glu Trp Glu Gly Val Phe Leu Ser Ser Gly Trp Lys Gly
65 70 75 80

Asn Thr Leu Ser Asn Tyr Tyr Ile Ser Leu Val Phe Tyr Tyr Ser Arg
85 90 95

Ile Leu Gln Pro Tyr Phe Tyr Cys Leu Trp Gly Lys Leu Glu Met Val
100 105 110

Thr Leu Ile Arg Ser Val Trp Arg Gly Ile Asn Gly Gly Asp Lys Ile
115 120 125

Ser Val Gly Phe Gly Lys Cys
130 135

<210> 318
<211> 38
<212> PRT
<213> Homo sapiens

<400> 318
Trp Met Glu Arg Lys His Thr Val Lys Leu Leu Tyr Leu Leu Gly Phe
1 5 10 15

Leu Leu Gln Asn Ser Pro Ala Ile Phe Leu Leu Ser Met Gly Glu Val
20 25 30

Gly Asp Gly Asp Leu Asp
35

<210> 319
<211> 23
<212> PRT
<213> Homo sapiens

<400> 319
Ser Asn Gly Glu Ser Ala Leu Lys Gly Thr Arg Pro Thr Phe Ser Ser
1 5 10 15

Pro Phe Ile Leu Val Thr Glu
20

<210> 320
<211> 24
<212> PRT
<213> Homo sapiens

<400> 320
Leu Ser Asn Tyr Tyr Ile Ser Leu Val Phe Tyr Tyr Ser Arg Ile Leu
1 5 10 15

Gln Pro Tyr Phe Tyr Cys Leu Trp
20

<210> 321
<211> 131
<212> PRT
<213> Homo sapiens

<400> 321
Glu Lys Asp Phe Met Gln Gly Ser Asp Ala Gly His Gly Gly Thr His
1 5 10 15

Ile Tyr Arg Ala Leu Val Gln Trp Pro Leu Ala Trp Val Phe Tyr Leu
20 25 30

Ser His Ala Lys Thr His Trp Gly Glu Glu Leu Arg Phe Ser Phe Arg
35 40 45

Arg Lys Asn Leu Arg Leu Arg Glu Ala Met Arg His Glu Thr Cys Gln
50 55 60

Val Thr Gln Leu Val Ala Gly Lys Ala Asp Ser Asn Leu Cys Leu Arg
65 70 75 80

Asp Ser Glu Thr Trp Phe Trp Pro Pro Leu Trp Ala Ala Cys Ser Ser
85 90 95

Leu Gln Ala Thr Ala Cys Arg Leu Ser Ser Pro Ser Lys Gly Leu Gly
100 105 110

```
Ala Ser Arg Glu Cys Pro Trp Leu Ala Ser Gly Arg Ala Ala Leu Val
        115                 120                 125

Ser Phe Leu
    130
```

<210> 322
<211> 69
<212> PRT
<213> Homo sapiens

<400> 322
```
Ser Leu Arg Val Lys Gly Arg Lys Pro Arg Leu Leu Tyr His Ser Pro
  1               5                  10                  15

Ala Arg Gly Thr Leu Trp Met Leu Pro Gly Leu Cys Asp Cys Leu Ile
             20                  25                  30

Cys Arg Gln Trp Leu Val Glu Arg Ser Arg Leu Pro Arg Val Gly Ala
         35                  40                  45

Arg Thr Arg Phe Gln Ser Pro Ser Asp Thr Gly Trp Ser Gln Leu Cys
     50                  55                  60

Gln Leu Pro Ala Val
 65
```

<210> 323
<211> 26
<212> PRT
<213> Homo sapiens

<400> 323
```
Glu Arg Ser Arg Leu Pro Arg Val Gly Ala Arg Thr Arg Phe Gln Ser
  1               5                  10                  15

Pro Ser Asp Thr Gly Trp Ser Gln Leu Cys
             20                  25
```

<210> 324
<211> 33
<212> PRT
<213> Homo sapiens

<400> 324
```
Lys His Ala Phe Leu Met Ala His Gln Phe Cys Val Leu Ser Leu Ala
  1               5                  10                  15

Met Gln Trp Ser Ser Cys Phe Gln Leu Val Ala Leu Pro Tyr Leu Ser
             20                  25                  30

Leu
```


<210> 325
<211> 51
<212> PRT
<213> Homo sapiens

<400> 325
```
Met Arg Pro Leu Cys Val Leu Leu Pro Trp Pro Cys Trp Gln Trp Gly
  1               5                  10                  15

Gly Leu Gly Ser Ala Ser Pro Ile Arg Pro Gln Ala Pro Pro Gly Gln
             20                  25                  30

Ala Ala His Ala Val Pro Leu Pro Arg Ala Gln His Leu Ala Gln Arg
         35                  40                  45

Ser Arg Gln
     50
```

<210> 326
<211> 52
<212> PRT
<213> Homo sapiens

<400> 326
```
Ala Arg Gly Leu Arg Ser Pro His Gly Ala Ala Gly Val Val Arg Gly
  1               5                  10                  15

Asp Gly Gly Gly Lys Lys Gly Glu Asp Pro Tyr Ser Pro Ile Leu Phe
             20                  25                  30

Gln Ser Glu Arg Ile Pro Arg Leu Ile Tyr Leu Pro Val Ile Ser Ser
         35                  40                  45

Glu Glu Asn Ser
     50
```

<210> 327
<211> 57
<212> PRT
<213> Homo sapiens

<400> 327
```
Lys Ser Leu Ser Cys Ser Phe Leu Phe Leu Ala Phe Trp Leu Arg Arg
  1               5                  10                  15

Met Gly Gln Thr Met Cys Val Cys Val Cys Val Cys Val Cys Val Cys
             20                  25                  30

Val Arg Thr Trp Val Tyr Leu Tyr Glu Pro Val Lys Phe Arg Ser Pro
         35                  40                  45

Leu Ile Tyr Val Asn Leu Pro Thr Ser
     50                  55
```

<210> 328

<211> 80
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (15)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 328
Lys Leu Gly Phe Thr Met Leu Ala Arg Leu Val Ser Asn Ser Xaa Thr
1 5 10 15

Ser Gly Asp Leu Pro Ser Ser Ala Ser Gln Asn Ala Gly Ile Lys Gly
20 25 30

Met Ser Tyr Arg Ala Trp Pro Tyr Ser Tyr Phe Leu Ile Arg Lys Asn
35 40 45

Lys Gln Thr Asn Lys Gln Thr Lys Thr Asn Pro Gln Leu Gly Glu Asn
50 55 60

Lys His Cys Arg Asn Leu Lys Val Ser Trp Ser Lys Asn Tyr Phe Leu
65 70 75 80

<210> 329
<211> 27
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (25)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 329
Glu Arg Gly Gln Gly Gly Ser Ser Arg Asn Val Ala Gly Ser Asp Leu
1 5 10 15

Val Phe Pro Ala Val Phe Val Ser Xaa Leu Cys
20 25

<210> 330
<211> 166
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (90)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>

<221> SITE
<222> (92)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (96)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (113)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (126)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (141)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (150)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 330
Gly Ser Pro Gln Gly Pro Ser Val Ala Leu Gly Ser Arg Gln Cys Trp
1 5 10 15

Ser Arg Pro Leu Arg Arg Gly Gly Arg Gly Ala Ala Val Glu Met Trp
20 25 30

Arg Gly Pro Thr Trp Cys Phe Arg Pro Ser Leu Cys Leu Cys Cys Val
35 40 45

Cys Gly Val Ser Phe Gly Leu Tyr Val Pro His Gly Phe Ser Leu Ser
50 55 60

Met Cys Val Ser Ala Pro Gly Ser Ala Trp Leu Ser Leu Val Tyr Ser
65 70 75 80

Ile Cys Leu Ala Arg Gly Ser Met Ser Xaa Arg Xaa Ser Ser Arg Xaa
85 90 95

Ser Leu Val Ala Ser Gly Ala Ser Val Leu Leu Val Cys Phe Trp Val
100 105 110

Xaa Ala Asp Pro Gly Val Gly Val Ser Val Pro Arg Ala Xaa Val Ser
115 120 125

Gly Leu Trp Trp Cys Val Ser Pro Ser Ala Cys Leu Xaa Leu Ala Pro
130 135 140

Thr Lys Pro Pro Pro Xaa Leu Ser Phe Ser Leu Ser Ile Phe Pro Phe

145 150 155 160

Ser Ser Asn Pro Ser Lys
165

<210> 331
<211> 118
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (31)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (39)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (55)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (67)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (84)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (89)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (90)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 331
Thr Ile Ala Ser Leu Gln Pro Thr Ala Leu Asn His Leu Ile Trp Arg
1 5 10 15

Gly Trp Lys Arg Lys Gly Arg Leu Arg Glu Arg Lys Arg Gly Xaa Gly
20 25 30

Gly Ala Trp Leu Gly Pro Xaa Arg Gly Arg Gln Met Asp Ser His Thr
35 40 45

Thr Arg Asp Gln Arg Gln Xaa Leu Gly Glu Gln Arg His Pro Leu Leu
50 55 60

Gly Leu Xaa Ala Pro Arg Ser Lys Pro Thr Lys Gln Met Pro Gln Met
65 70 75 80

Gln Pro Gly Xaa Pro Glu Lys Lys Xaa Xaa Leu Thr Trp Asn His Gly
85 90 95

Leu Asp Arg Trp Asn Thr Gln Gly Thr Ala Arg Gln Ser Leu Gly Gln
100 105 110

Lys His Thr Trp Arg Asp
115

<210> 332
<211> 21
<212> PRT
<213> Homo sapiens

<400> 332
Ala Arg Gly Pro Gly Thr Glu Gly Cys Glu Pro Trp Leu Gln Leu Gln
1 5 10 15

Asp Arg Arg Glu Arg
20

<210> 333
<211> 59
<212> PRT
<213> Homo sapiens

<400> 333
Met Ser Ser Gly Thr Asn Ser Phe Phe Thr Leu Met Ala Leu Asn Ser
1 5 10 15

Pro Thr Gly Asp Ser Gly Ser Arg Ile Thr Val Ser Pro Pro Arg Val
20 25 30

His Pro Val Lys Ser Gly Arg Gly Arg Ala Ser Asp Leu Leu Leu Thr
35 40 45

Arg Phe Leu Ala Pro Arg Ser Ala Leu Trp Ser
50 55

<210> 334
<211> 26
<212> PRT
<213> Homo sapiens

<400> 334
His Glu Tyr His Leu Leu Ser Ser Arg His Ile Leu Gly Ser Val Leu
1 5 10 15

Arg Leu Asp Val Cys Ser Ala Leu Trp Ser
20 25

<210> 335
<211> 82
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (44)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (54)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (59)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (67)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 335
Phe Ile Leu Phe Ile Leu Glu Tyr Asp Met Leu Trp Lys Ser Leu Tyr
1 5 10 15

Thr Asn Ser Ser Ala Tyr Gly Tyr Val Ile Ala Ser Tyr Phe Cys Leu
20 25 30

Leu Gly Ile Lys Leu Leu Val Lys Gln Lys Lys Xaa Lys Lys Lys Thr
35 40 45

Arg Gly Gly Ala Arg Xaa Pro Ile Arg Pro Xaa Val Glu Ser Tyr Tyr
50 55 60

Lys Ser Xaa Ala Val Val Leu Gln Arg Arg Gly Leu Gly Lys Asn Leu
65 70 75 80

Gly Gly

<210> 336
<211> 102
<212> PRT
<213> Homo sapiens

<400> 336
Arg Val Ser Ser His Leu Phe Arg Leu Phe Gly Gly Leu Ile Leu Asp
1 5 10 15

Ile Lys Arg Lys Ala Pro Phe Phe Leu Ser Asp Phe Lys Asp Ala Leu
20 25 30

Ser Leu Gln Cys Leu Ala Ser Ile Leu Phe Leu Tyr Cys Ala Cys Met
35 40 45

Ser Pro Val Ile Thr Phe Gly Gly Leu Leu Gly Glu Ala Thr Glu Gly
50 55 60

Arg Ile Val Ser Thr Lys Ile Gly Ser Gly Gln Ala Phe Ser Ser Ser
65 70 75 80

Glu Ala Ser Val Cys Met His Leu Ser His Tyr Ser Tyr Phe Tyr Leu
85 90 95

Lys Ser Leu Pro Thr Ala
100

<210> 337
<211> 24
<212> PRT
<213> Homo sapiens

<400> 337
Phe Arg Leu Phe Gly Gly Leu Ile Leu Asp Ile Lys Arg Lys Ala Pro
1 5 10 15

Phe Phe Leu Ser Asp Phe Lys Asp
20

<210> 338
<211> 23
<212> PRT
<213> Homo sapiens

<400> 338
Phe Leu Tyr Cys Ala Cys Met Ser Pro Val Ile Thr Phe Gly Gly Leu
1 5 10 15

Leu Gly Glu Ala Thr Glu Gly
20

<210> 339
<211> 22
<212> PRT
<213> Homo sapiens

<400> 339
Ser Ser Ser Glu Ala Ser Val Cys Met His Leu Ser His Tyr Ser Tyr
1 5 10 15

Phe Tyr Leu Lys Ser Leu
20

<210> 340
<211> 106
<212> PRT

<213> Homo sapiens

<400> 340
Pro Cys Leu Gln Val Ile Gly Ile Asp Phe Cys Arg Leu Leu Leu Met
1 5 10 15

Cys Leu Val Leu Lys Arg Asn Leu Thr Val Pro Phe Ser Ser Tyr Ser
20 25 30

Pro Leu Lys Thr Ile Thr Cys Ile Thr Ser Glu Gln Ile Ala Val Val
35 40 45

Ser Asn Phe Phe Arg Gln Lys Leu Gly Val Arg Ala Lys Phe Phe Gln
50 55 60

Gly Ala Cys Leu His Thr Ser Lys Val Val Ile Cys Leu Asn Leu Pro
65 70 75 80

Ile Ile Ser Ile Gln Arg Ala Asp Ile Arg Met Trp Trp Leu Val Val
85 90 95

Asn Thr Pro Tyr Ala Arg Gly Val Asn Asn
100 105

<210> 341
<211> 21
<212> PRT
<213> Homo sapiens

<400> 341
Val Val Ser Val Cys Val Leu Glu Thr Gly Gln Leu Gly Pro Ala Ala
1 5 10 15

Leu Cys Arg Ser Val
20

<210> 342
<211> 97
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (28)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (79)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (83)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (85)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (90)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 342
Asn Ile Ser Val His Gly Phe Pro Val Pro Cys Leu Arg Gln Arg Leu
1 5 10 15

Gln Gly Pro Cys His Pro Lys Cys Cys Pro His Xaa Ile Ser Ser Gly
20 25 30

Lys Pro Arg Ser Ser Phe Ser Pro Ser Ser Tyr His Cys Lys Phe Ser
35 40 45

Arg Asn Ala Thr Leu Leu Val Val Pro Asn Ile Phe Ser Tyr Met Gln
50 55 60

Ser Ser Phe Leu Ile Pro Gln Thr Ser Lys Tyr Tyr Ile Leu Xaa Pro
65 70 75 80

Tyr Ala Xaa Thr Xaa Arg Pro Ile Lys Xaa Ile Phe Lys Gln Ala Lys
85 90 95

Gln

<210> 343
<211> 58
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (19)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 343
Ile Tyr Asn Asp Met Met Met Glu Lys Lys Lys Thr Glu Val Tyr Gln
1 5 10 15

Lys Arg Xaa Ser Gly Asp Asn Thr Trp Gly Gly Lys Gly Leu Val Ala
20 25 30

Phe Val Ser Ser Met Glu Gln Gly Ile His Val Gln Arg Cys Phe Ile
35 40 45

Ala Asn Leu Lys Phe Ser Ser Pro Gly Val
50 55

<210> 344

<211> 93
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (16)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 344
Tyr Asp Asp Gly Glu Lys Glu Asp Arg Gly Leu Pro Glu Glu Met Xaa
1 5 10 15

Trp Gly Gln His Leu Gly Trp Gln Gly Pro Cys Ser Leu Cys Leu Lys
20 25 30

His Gly Thr Gly Asn Pro Cys Thr Glu Met Phe Tyr Cys Gln Phe Lys
35 40 45

Ile Phe Ile Ser Trp Cys Leu Ile Pro Leu Val Phe Ala Arg Leu Gly
50 55 60

Asp Phe Arg Asp Arg Pro Gly Trp Ile Phe Ser Trp Arg Tyr His Leu
65 70 75 80

Lys His Thr Val Trp Gly Gly Tyr Asn Ile Ile Met Leu
85 90

<210> 345
<211> 21
<212> PRT
<213> Homo sapiens

<400> 345
Thr Pro Gly Asp Glu Asn Phe Lys Leu Ala Ile Lys His Leu Cys Thr
1 5 10 15

Trp Ile Pro Cys Ser
20

<210> 346
<211> 34
<212> PRT
<213> Homo sapiens

<400> 346
Ile Arg His Glu Ile Phe Leu Thr Ile Glu Ser Phe Cys Pro Ser Ala
1 5 10 15

Pro Arg Gly Glu Asp Asp Asp Asn Leu Leu Arg Thr Ser Arg Val Pro
20 25 30

Asp Ile

<210> 347
<211> 160
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (126)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (130)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 347
Ile Arg Gly Ser Ile Pro Gly His Lys Lys Met His Leu Ser Phe Asn
1 5 10 15

Val Ala Ala Gln Trp Ser Leu Leu Lys Pro Leu Val Leu Arg Glu Glu
20 25 30

Gly Ala Leu Phe Leu Thr His Asp Gln Leu Glu Ser Lys Asn Ser Trp
35 40 45

Thr Leu Ser Ile Gly Pro Arg Val Pro Tyr Thr Tyr Val Val Val Thr
50 55 60

Trp Ser Ser Ala Leu Trp Asp Leu Pro Asn Gln Pro Leu Ala Gly Arg
65 70 75 80

Lys Glu Ser Gly Gly Ser Tyr Gly Pro Ile Ser Val Thr Gln Ser Pro
85 90 95

His Gln Ala Ala Leu Lys Trp Phe Ala Lys Lys Lys Gly Lys Gln Ser
100 105 110

His Ser Thr Val Gln Leu Ala Asn Ile Leu His Val Phe Xaa Ala Pro
115 120 125

Asp Xaa Tyr His Phe Val Asn Thr Ser Leu Gln Leu Phe Leu Glu Tyr
130 135 140

Thr Val Met Cys Met Leu Cys Glu Asn Lys Gln Lys Thr Leu Gly Arg
145 150 155 160

<210> 348
<211> 135
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (8)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (10)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 348
Glu Pro Glu Val Thr Gln Val Xaa Ser Xaa Glu Leu Thr Phe Gln Pro
1 5 10 15

Arg Lys Ala Gly Ala Lys Val Thr Ala Gly Lys Ser His His Gln Val
20 25 30

Ile His Trp Glu Phe Glu Ile Met Leu Ser Ser Tyr Ser Thr Asp Val
35 40 45

Pro Leu Trp Phe Leu Lys Phe Phe Ser Ser Asn Leu Pro Gln Thr Tyr
50 55 60

Phe Pro His Ser Gly Val Lys Lys Trp Gly Ser Cys Phe Ser Leu Pro
65 70 75 80

Trp Arg Asp Ser Pro Pro Leu Thr Phe Ile Ser Leu Leu Ser Ser His
85 90 95

Leu Thr Thr Phe His Leu Tyr His Leu His His Gly Ile Ile Cys Leu
100 105 110

Gly Phe Ser Val Tyr Phe His Arg Ala Tyr Thr Ser Leu Cys Ile Leu
115 120 125

Glu Thr Ala Val Gly Ser Tyr
130 135

<210> 349
<211> 25
<212> PRT
<213> Homo sapiens

<400> 349
Trp Ser Leu Leu Lys Pro Leu Val Leu Arg Glu Glu Gly Ala Leu Phe
1 5 10 15

Leu Thr His Asp Gln Leu Glu Ser Lys
20 25

<210> 350
<211> 22
<212> PRT
<213> Homo sapiens

<400> 350
Trp Phe Ala Lys Lys Lys Gly Lys Gln Ser His Ser Thr Val Gln Leu
1 5 10 15

Ala Asn Ile Leu His Val
20

<210> 351
<211> 25
<212> PRT
<213> Homo sapiens

<400> 351
Ala Gly Lys Ser His His Gln Val Ile His Trp Glu Phe Glu Ile Met
1 5 10 15

Leu Ser Ser Tyr Ser Thr Asp Val Pro
20 25

<210> 352
<211> 26
<212> PRT
<213> Homo sapiens

<400> 352
His Gly Ile Ile Cys Leu Gly Phe Ser Val Tyr Phe His Arg Ala Tyr
1 5 10 15

Thr Ser Leu Cys Ile Leu Glu Thr Ala Val
20 25

<210> 353
<211> 19
<212> PRT
<213> Homo sapiens

<400> 353
Lys Arg Leu Thr Ile Asn Ala Arg Val His Leu Trp Thr Leu Lys Ser
1 5 10 15

Val Pro Leu

<210> 354
<211> 72
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (7)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (8)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 354
Glu Tyr Val Phe Asn Met Xaa Xaa Tyr Ser Lys Ser Arg Ala Ile Ser
1 5 10 15

Pro Leu Ser Gly Pro Tyr Thr Pro Arg Gly Thr Thr Pro Leu Pro Ile
20 25 30

Ile Pro Glu Pro Gly Ala Arg Gln Arg Asp His Pro Ala Ser Leu Lys
35 40 45

Tyr Ala Lys Ile Ile Gln Thr Lys Leu Phe Ala Leu Pro Tyr Pro Lys
50 55 60

Glu Thr Ser Met Lys Ala Val Ala
65 70

<210> 355
<211> 65
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (15)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (25)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (26)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 355
Glu Thr Val Pro Pro Arg Ser Ser Gln Phe Leu Lys Ile Thr Xaa Gly
1 5 10 15

Pro Ala Arg Ser Met Ser Leu Ile Xaa Xaa Ala Ile Gln Asn Pro Glu
20 25 30

Pro Tyr Leu Leu Tyr Leu Ala Leu Ile Pro Gln Glu Ala Leu Leu Leu
35 40 45

Tyr Leu Ser Ser Gln Ser Gln Val Pro Gly Asn Glu Thr Thr Pro Pro
50 55 60

Val
65

<210> 356
<211> 101
<212> PRT
<213> Homo sapiens

<400> 356
Asn Glu Val Ser Phe Ser Leu Ser Leu Gly Phe Ser Pro Arg Glu Phe
1 5 10 15

Ala Arg Trp Lys Val Asn Asn Leu Ala Leu Glu Arg Lys Asp Phe Phe
20 25 30

Ser Leu Pro Leu Pro Leu Ala Pro Glu Phe Ile Arg Asn Ile Arg Leu
35 40 45

Leu Gly Arg Arg Pro Asn Leu Gln Gln Val Thr Glu Asn Leu Ile Lys
50 55 60

Lys Tyr Gly Thr His Phe Leu Leu Ser Ala Thr Leu Gly Gly Lys Gln
65 70 75 80

His His Asn Pro Lys Leu Ile Gly Cys Gln Thr Ile Gly Asn Asn Val
85 90 95

Lys Thr Arg Val Ala
100

<210> 357
<211> 75
<212> PRT
<213> Homo sapiens

<400> 357
Val Pro Tyr Phe Leu Ile Arg Phe Ser Val Thr Cys Cys Arg Leu Gly
1 5 10 15

Leu Leu Pro Arg Arg Arg Met Phe Arg Ile Asn Ser Gly Ala Arg Gly
20 25 30

Asn Gly Lys Leu Lys Lys Ser Phe Leu Ser Arg Ala Lys Leu Phe Thr
35 40 45

Phe Gln Arg Ala Asn Ser Leu Gly Glu Lys Pro Arg Asp Lys Glu Lys
50 55 60

Leu Thr Ser Phe Gln Ser Lys Arg His Lys Ile
65 70 75

<210> 358
<211> 63
<212> PRT
<213> Homo sapiens

<400> 358
Glu Met Ser Ala Val Leu Phe Asn Gln Ile Phe Cys Asn Leu Leu Gln
1 5 10 15

Ile Gly Ser Pro Ser Lys Glu Ala Asn Val Pro Asp Lys Leu Trp Gly
20 25 30

Lys Arg Gln Trp Gln Thr Glu Glu Val Leu Pro Phe Gln Ser Gln Val
35 40 45

Val His Leu Pro Thr Gly Lys Leu Pro Gly Gly Lys Ala Lys Gly
50 55 60

<210> 359
<211> 99
<212> PRT
<213> Homo sapiens

<400> 359
His Tyr His Gly Ser Gly Phe Leu Ile Lys Glu Phe Gly Ser Phe Leu
1 5 10 15

Ser Leu Leu Cys Met Leu Ser Cys Pro Tyr Val Phe Cys His Gly Met
20 25 30

Leu Glu Gln Glu Val Pro Ser Ser Val Val Ser Pro Ser Thr Leu Asp
35 40 45

Phe Pro Thr Ser Arg Thr Val Asn Lys Phe Leu Phe Lys Leu Pro Ser
50 55 60

Leu Trp Tyr Ser Val Ile Ala Thr Gln Asn Gly Leu Lys Gln Lys Ile
65 70 75 80

Arg Glu Thr Phe Leu Phe Val Gln Phe Ser Gln Met Pro Arg Trp His
85 90 95

Lys Leu Glu

<210> 360
<211> 48
<212> PRT
<213> Homo sapiens

<400> 360
Phe Cys Lys His Asn Gly Ser Lys Asn Val Phe Ser Thr Phe Arg Thr
1 5 10 15

Pro Ala Val Leu Phe Thr Gly Ile Val Ala Leu Tyr Ile Ala Ser Gly
20 25 30

Leu Thr Gly Phe Ile Gly Leu Glu Val Val Ala Gln Leu Phe Asn Cys
35 40 45

<210> 361
<211> 139
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (28)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (115)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 361
Met Pro Lys Pro Gly Ala Ala Thr Gln Arg Thr Leu Leu Cys Leu Pro
1 5 10 15

Arg Leu His Pro Ala Ser Gly Pro Pro Leu Pro Xaa Ala Gly Pro Leu
20 25 30

Arg Gly Leu Arg Gln Leu Pro Ala Leu Pro Val Pro Ala Ala Ser Cys
35 40 45

Arg Arg Arg Pro Ala Pro Arg Leu Cys Ala Ala Gly Pro Cys Thr Val
50 55 60

Gly Pro Ala Ala Ser Pro His Ala Pro Pro His Gly Cys Pro Pro Pro
65 70 75 80

Ala Ser Leu Ala His Val Ala His Arg Gln Ser Val Ser Gly Thr Val
85 90 95

Cys Leu Gly Leu Arg Asp Gly His Val Arg Gly Gly Cys Ala Ala Val
100 105 110

Arg Gly Xaa Ala Ala Leu Pro Trp Asp Ala Ala Ala Ala Gly Pro Asp
115 120 125

His Met Gly Val Gly Ser Gly Pro Ala Leu Leu
130 135

<210> 362
<211> 35
<212> PRT
<213> Homo sapiens

<400> 362
Met Trp Gly Gln Pro Arg Pro Val Asp Ser Val Trp Ser Ser Ser Ile
1 5 10 15

Pro Lys Lys Ser Val Glu Ser Asn Asp Asn Lys Ser His Leu His Lys
20 25 30

Arg Glu His
35

<210> 363
<211> 26

<212> PRT
<213> Homo sapiens

<400> 363
Met Thr Thr Lys Ala Ile Phe Thr Lys Gly Asn Ile Asp Ser Leu Ser
1 5 10 15

Phe Lys Ser Asn Met Trp Ser Val Tyr Ile
20 25

<210> 364
<211> 26
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (3)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 364
Asp Ser Xaa Leu Asp Arg Arg Pro Ser Gly Pro Asp Val Lys Phe Leu
1 5 10 15

Ser Asn Lys His His Phe Ser Met Val Cys
20 25

<210> 365
<211> 84
<212> PRT
<213> Homo sapiens

<400> 365
Cys Leu Ala Glu Ala Val Ser Val Ile Gln Ser Ile Pro Ile Phe Asn
1 5 10 15

Glu Thr Gly Arg Phe Ser Phe Thr Leu Pro Tyr Pro Val Lys Ile Lys
20 25 30

Val Arg Phe Ser Phe Phe Leu Gln Ile Tyr Leu Ile Met Ile Phe Leu
35 40 45

Gly Leu Tyr Ile Asn Phe Arg His Leu Tyr Lys Gln Arg Arg Arg Arg
50 55 60

Tyr Gly Gln Lys Lys Lys Arg Ser Thr Lys Lys Lys Asp Leu Asp Gly
65 70 75 80

Phe Leu Pro Val

<210> 366
<211> 62
<212> PRT
<213> Homo sapiens

<400> 366
Leu Cys Ser Thr Pro Val Pro Thr Leu Phe Cys Pro Arg Ile Val Leu
1 5 10 15

Glu Val Leu Val Val Leu Arg Ser Ile Ser Glu Gln Cys Arg Arg Val
20 25 30

Ser Ser Gln Val Thr Val Ala Ser Glu Leu Arg His Arg Gln Trp Val
35 40 45

Glu Arg Thr Leu Arg Ser Arg Gln Arg Gln Asn Tyr Leu Arg
50 55 60

<210> 367
<211> 48
<212> PRT
<213> Homo sapiens

<400> 367
Ala Arg Gly Glu Thr Ala Tyr Asp Gly Ala Ala Val Glu Phe Gln Glu
1 5 10 15

Pro Leu Ser Ser Cys Leu Phe Ser Ser Leu Asn Pro His His Trp Pro
20 25 30

Thr Leu Gly Val Gly Arg Pro Val Met Leu Thr Leu Glu Asp Lys Asp
35 40 45

<210> 368
<211> 200
<212> PRT
<213> Homo sapiens

<400> 368
Glu Leu Leu Gln Cys Gln Met Leu Glu Ala Ser Thr Leu Ile His Leu
1 5 10 15

His His Pro Arg Pro Gly Phe Pro Ala Leu Cys Ser Phe Leu Gly Phe
20 25 30

Arg His His Leu His His Asp Ala Leu Cys Ile Arg Val Leu Pro Glu
35 40 45

Asp Leu Glu Ala Lys Leu Cys Val Ser Leu His Gln Leu Leu His Arg
50 55 60

Gly Leu Cys Leu Pro Gly Phe Gly Ala Ala Cys Pro Gly Asp Gln Gly
65 70 75 80

Ser Glu Asp Glu Ala Arg Pro Pro Ala Val Leu Arg Ala Val Ala Leu
85 90 95

```
Leu Arg Ala Gly Leu Arg His Leu Ser Val His Ser Gly Trp Tyr His
            100                 105                 110

Leu Pro His Ser Arg Asn Gly Leu Pro Leu Leu Ala Leu Val Val His
        115                 120                 125

Phe Pro Glu Tyr Gly Gly Gly Pro Arg Glu Pro Val Pro Gly Gln Ser
    130                 135                 140

Gly Glu Phe Gly Arg Arg Thr Glu Leu Ser Thr Lys Gly Asp Thr Gly
145                 150                 155                 160

Asp Ser Arg Asn Ser His Leu Ala Gln Asp Met Ala Ser Leu Pro Phe
                165                 170                 175

Phe Lys Pro Cys Glu Cys Thr His Val Ala Val Cys Ser Pro Pro His
            180                 185                 190

Pro Leu Cys Gln Tyr Leu Cys Leu
        195                 200
```

<210> 369
<211> 28
<212> PRT
<213> Homo sapiens

<400> 369
```
Leu Gln Cys Gln Met Leu Glu Ala Ser Thr Leu Ile His Leu His His
  1               5                  10                  15

Pro Arg Pro Gly Phe Pro Ala Leu Cys Ser Phe Leu
            20                  25
```

<210> 370
<211> 31
<212> PRT
<213> Homo sapiens

<400> 370
```
His Gln Leu Leu His Arg Gly Leu Cys Leu Pro Gly Phe Gly Ala Ala
  1               5                  10                  15

Cys Pro Gly Asp Gln Gly Ser Glu Asp Glu Ala Arg Pro Pro Ala
            20                  25                  30
```

<210> 371
<211> 27
<212> PRT
<213> Homo sapiens

<400> 371
```
Leu Ala Leu Val Val His Phe Pro Glu Tyr Gly Gly Gly Pro Arg Glu
  1               5                  10                  15

Pro Val Pro Gly Gln Ser Gly Glu Phe Gly Arg
```



```
            20                  25
```

<210> 372
<211> 30
<212> PRT
<213> Homo sapiens

<400> 372
```
Gln Ser Trp Thr Ala Pro Ala Ala Arg Leu Pro Met Ala Leu Pro Gln
  1               5                  10                  15

Met Cys Asp Gly Ser His Leu Ala Ser Thr Leu Arg Tyr Cys
            20                  25                  30
```

<210> 373
<211> 190
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (32)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (47)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 373
```
Gln Ser Ala Ala Gln Trp Phe Trp Trp Pro Gly Arg Ser Ala Ser Leu
  1               5                  10                  15

Gly Gly Ala Lys Gly Met Gln Pro Pro Ser Leu Ala Ser Trp Pro Xaa
            20                  25                  30

Pro Arg Ser Ile Arg Cys Leu Arg Ala Pro Ala Pro Cys Ser Xaa Pro
        35                  40                  45

Ser Ala Ser Ser Ala Ala Val Gln Val Ala Cys Cys Cys Ser Leu Ala
    50                  55                  60

Cys Cys Gly Pro Ser Arg Pro Ala Ser Gln Gly His Leu Arg Trp Asp
65                  70                  75                  80

Pro Tyr His Leu Ser Arg Asp Leu Tyr Tyr Leu Thr Val Glu Ser Ser
                85                  90                  95

Glu Lys Glu Ser Cys Arg Thr Pro Lys Val Val Asp Ile Pro Thr Tyr
            100                 105                 110

Glu Glu Ala Val Ser Phe Pro Val Ala Glu Gly Pro Pro Thr Pro Pro
        115                 120                 125

Ala Tyr Pro Thr Glu Glu Ala Leu Glu Pro Ser Gly Ser Arg Asp Ala
    130                 135                 140
```

```
Leu Leu Ser Thr Gln Pro Ala Trp Pro Pro Pro Ser Tyr Glu Ser Ile
145                 150                 155                 160

Ser Leu Ala Leu Asp Ala Val Ser Ala Glu Thr Thr Pro Ser Ala Thr
                165                 170                 175

Arg Ser Cys Ser Gly Leu Val Gln Thr Ala Arg Gly Gly Ser
            180                 185                 190
```

<210> 374
<211> 93
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (59)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 374
```
Gly Ser Thr Gly Leu Trp Arg Gly Asp Arg Gly Pro Ile Glu Gly Gly
  1               5                  10                  15

Pro Gly Met Leu Ala Leu Thr Asp His Ser Arg Pro Met Ser Ser Ser
            20                  25                  30

Arg Pro Pro Ala Pro Gln Gln Thr Lys Leu Thr Asp Leu Ser Arg Gly
        35                  40                  45

Leu Gly Pro Ser Gly Thr Gly Tyr Ser Val Xaa Gly Ala Ser Trp Pro
    50                  55                  60

Gly Trp Ala Val Ala Ser Pro Ser Leu His Gln Ala Lys Gln Ser Val
65                  70                  75                  80

Pro Ala Thr Arg Thr Thr Val Pro Leu Thr Val Met Gln
                85                  90
```

<210> 375
<211> 27
<212> PRT
<213> Homo sapiens

<400> 375
```
Gln Trp Phe Trp Trp Pro Gly Arg Ser Ala Ser Leu Gly Gly Ala Lys
  1               5                  10                  15

Gly Met Gln Pro Pro Ser Leu Ala Ser Trp Pro
            20                  25
```

<210> 376
<211> 29
<212> PRT
<213> Homo sapiens

<400> 376
```
Ser Ser Ala Ala Val Gln Val Ala Cys Cys Cys Ser Leu Ala Cys Cys
  1               5                  10                  15

Gly Pro Ser Arg Pro Ala Ser Gln Gly His Leu Arg Trp
            20                  25
```

<210> 377
<211> 32
<212> PRT
<213> Homo sapiens

<400> 377
```
Val Ser Phe Pro Val Ala Glu Gly Pro Pro Thr Pro Pro Ala Tyr Pro
  1               5                  10                  15

Thr Glu Glu Ala Leu Glu Pro Ser Gly Ser Arg Asp Ala Leu Leu Ser
            20                  25                  30
```

<210> 378
<211> 26
<212> PRT
<213> Homo sapiens

<400> 378
```
Arg Val Ser Phe Pro Val Ala Glu Gly Pro Pro Thr Pro Pro Ala Tyr
  1               5                  10                  15

Pro Thr Glu Glu Ala Leu Glu Pro Ser Gly
            20                  25
```

<210> 379
<211> 95
<212> PRT
<213> Homo sapiens

<400> 379
```
Ser Asn Glu Ile Leu Leu Ser Phe Pro Gln Asn Tyr Tyr Ile Gln Trp
  1               5                  10                  15

Leu Asn Gly Ser Leu Ile His Gly Leu Trp Asn Leu Ala Ser Leu Phe
            20                  25                  30

Ser Asn Leu Cys Leu Phe Val Leu Met Pro Phe Ala Phe Phe Phe Leu
        35                  40                  45

Glu Ser Glu Gly Phe Ala Gly Leu Lys Lys Gly Ile Arg Ala Arg Ile
    50                  55                  60

Leu Glu Thr Leu Val Met Leu Leu Leu Leu Ala Leu Leu Ile Leu Gly
65                  70                  75                  80
```

```
Ile Val Trp Val Ala Ser Ala Leu Ile Asp Asn Asp Ala Ala Ser
                85                  90                  95


<210> 380
<211> 33
<212> PRT
<213> Homo sapiens

<400> 380
Pro Thr Arg Pro Val Leu Leu Leu Ala Ile Asn Gly Val Thr Glu Cys
  1               5                  10                  15

Phe Thr Phe Ala Ala Met Ser Lys Glu Glu Val Asp Arg Tyr Asn Phe
            20                  25                  30

Val



<210> 381
<211> 93
<212> PRT
<213> Homo sapiens

<400> 381
Asn Asp Lys Lys Leu Leu Phe Leu Lys Gly Phe Trp Ser Ser Leu Lys
  1               5                  10                  15

Asn Glu Thr Pro Pro Pro His Phe Arg Leu Arg Met Val Thr Gly Val
            20                  25                  30

Ser Cys Ser Gly Thr Leu Trp Cys Leu Ile Ser Gly Val Ala Val Thr
        35                  40                  45

Pro Leu Gln Ser Pro Gln Trp Gly Ser Tyr Thr Glu Cys Val Pro Pro
    50                  55                  60

Thr Glu Leu Pro Ile Ala Gly Pro Gly Ala Ser Gly Val Gln Ala Ser
65                  70                  75                  80

Leu Lys Ser Arg His Phe Val Ser Ala Ser Gly His Thr
                85                  90


<210> 382
<211> 65
<212> PRT
<213> Homo sapiens

<400> 382
Ser Glu Asn Arg Ile Tyr Arg Asn Gly Leu Glu Lys Met Arg Arg Glu
  1               5                  10                  15

Val Thr Ile Gly Arg Ser Ser Ser Ile Cys Leu Asp Gln Gln Val Lys
            20                  25                  30
```



```
Ala Gly Asn Ala Val His His Gln Trp Leu Lys Tyr Val Cys Trp Met
        35                  40                  45

Val Val Val Val Gly Gly Ser Gly Val Gly Asp Gly Gly Asn Leu Gly
    50                  55                  60

Met
 65


<210> 383
<211> 129
<212> PRT
<213> Homo sapiens

<400> 383
Asn Trp Ser Gly Arg Arg Leu Arg Met Trp Pro Ser Ala Ala Leu Ser
  1               5                  10                  15

Pro Ala Val Ser Ser Pro Ala Leu Ala Leu Thr Ser Pro Pro Lys Pro
            20                  25                  30

Leu Lys Gly Glu Val Trp Leu Arg Trp Lys Leu Leu Gly Ser Arg Ala
        35                  40                  45

Val Gly Leu Phe Ala Phe Ile Ala Leu Gly Thr Gln Ser Pro Leu Leu
    50                  55                  60

His Arg Ala Cys Leu Pro Val Arg Gln Ser Trp Gly Cys Ser Glu His
65                  70                  75                  80

Lys Ala Tyr Pro Ile Leu Arg Leu Gln Pro Asp Leu Glu Thr Gln Val
                85                  90                  95

Gly Pro Gly His Gly Val Asn Trp Asp Leu Arg Thr Gln Ile Arg Thr
            100                 105                 110

Ile Gly Glu Leu Gly Gly Asp Gly Gly Cys Ser Glu Met Arg Pro Leu
        115                 120                 125

Phe



<210> 384
<211> 123
<212> PRT
<213> Homo sapiens

<400> 384
Asn Leu Phe Ser Thr Pro Cys Lys Arg Gln Lys Leu Ile Lys Leu Glu
  1               5                  10                  15

Trp Thr Glu Ala Pro Asn Val Ala Leu Arg Cys Ser Leu Ser Cys Ser
            20                  25                  30

Leu Ile Pro Gly Leu Ser Pro Asp Leu Ser Ser Glu Ala Pro Glu Gly
        35                  40                  45
```

```
Arg Ser Val Ala Lys Met Glu Ile Ala Arg Gln Gln Ser Cys Trp Leu
     50                  55                  60

Val Cys Ile Tyr Cys Phe Arg Asn Pro Glu Ser Thr Leu Ala Pro Gly
 65                  70                  75                  80

Leu Pro Ala Cys Glu Ala Glu Leu Gly Leu Leu Arg Ala Gln Gly Leu
                 85                  90                  95

Pro His Pro Ala Ser Pro Ala Arg Leu Gly Asn Thr Gly Gly Ala Trp
            100                 105                 110

Pro Arg Ser Lys Leu Gly Ser Gln Asn Thr Asn
        115                 120


<210> 385
<211> 26
<212> PRT
<213> Homo sapiens

<400> 385
Ser Ser Pro Ala Leu Ala Leu Thr Ser Pro Pro Lys Pro Leu Lys Gly
  1               5                  10                  15

Glu Val Trp Leu Arg Trp Lys Leu Leu Gly
             20                  25


<210> 386
<211> 28
<212> PRT
<213> Homo sapiens

<400> 386
Glu His Lys Ala Tyr Pro Ile Leu Arg Leu Gln Pro Asp Leu Glu Thr
  1               5                  10                  15

Gln Val Gly Pro Gly His Gly Val Asn Trp Asp Leu
             20                  25


<210> 387
<211> 28
<212> PRT
<213> Homo sapiens

<400> 387
Ala Leu Arg Cys Ser Leu Ser Cys Ser Leu Ile Pro Gly Leu Ser Pro
  1               5                  10                  15

Asp Leu Ser Ser Glu Ala Pro Glu Gly Arg Ser Val
             20                  25


<210> 388
<211> 73
```



```
<212> PRT
<213> Homo sapiens

<400> 388
Leu Ala Pro Glu Cys Cys Cys Gly Ser Val Thr Tyr Pro Arg Ala Leu
  1               5                  10                  15

Val Pro Arg Pro Cys Cys Pro Glu Pro Arg Ala Pro Leu Gln Leu Thr
             20                  25                  30

Leu Gly Leu Phe Ser Ala Asn Pro Val Asn Ala Ser Pro Trp Gly Arg
         35                  40                  45

Cys Arg Ser Arg Arg Gly Arg Gly Asn Leu Pro Leu Gly His Pro Val
     50                  55                  60

Ser Thr Ala Phe Ser Ser Gly Asp Ser
 65                  70


<210> 389
<211> 102
<212> PRT
<213> Homo sapiens

<400> 389
Asn Thr Leu His Ser Lys Leu Val Pro Ser Val Tyr His Ser Thr Glu
  1               5                  10                  15

Lys Ser Cys Leu Val Cys Phe Gly Met Cys Pro Ser Ile Tyr Lys Lys
             20                  25                  30

Met Lys Ser Val Leu Leu Ile Gly Thr Arg Met Leu Leu Trp Leu Ser
         35                  40                  45

His Ile Ser Gln Gly Pro Arg Pro Glu Ala Val Leu Pro Arg Ala Pro
     50                  55                  60

Ser Pro Ser Ala Ala His Pro Trp Leu Val Phe Arg Lys Pro Gly Lys
 65                  70                  75                  80

Arg Lys Pro Leu Gly Gln Met Gln Lys Gln Lys Arg Glu Gly Lys Pro
                 85                  90                  95

Ala Ser Gly Ser Pro Cys
            100


<210> 390
<211> 25
<212> PRT
<213> Homo sapiens

<400> 390
Tyr Pro Arg Ala Leu Val Pro Arg Pro Cys Cys Pro Glu Pro Arg Ala
  1               5                  10                  15

Pro Leu Gln Leu Thr Leu Gly Leu Phe
```

20 25

<210> 391
<211> 27
<212> PRT
<213> Homo sapiens

<400> 391
Val Leu Leu Ile Gly Thr Arg Met Leu Leu Trp Leu Ser His Ile Ser
1 5 10 15

Gln Gly Pro Arg Pro Glu Ala Val Leu Pro Arg
20 25

<210> 392
<211> 61
<212> PRT
<213> Homo sapiens

<400> 392
Trp Ile Ile Val Met Phe Gly Lys Val Leu Lys Ile Lys Asp Phe Met
1 5 10 15

Ser Thr Tyr Ser His Thr Tyr Thr His Thr His Met His Ala His Thr
20 25 30

His Thr His Thr Leu Thr Leu Ser Leu Leu Gln Asn Val Leu Thr Leu
35 40 45

Val Ala Ile Ser Asp Ser Asp Lys Ala Leu Leu Ile Phe
50 55 60

<210> 393
<211> 69
<212> PRT
<213> Homo sapiens

<400> 393
Met Thr Leu Leu Ile Ala Glu Lys Thr Trp Arg Arg Pro Trp Pro Cys
1 5 10 15

Gln Trp Gly Tyr Leu Gly Ala Glu Gly Asp Arg His Leu Glu Gly Arg
20 25 30

Ser Leu Ser Leu Arg His Leu Gln Gly Ala Glu Thr Pro Val Leu Asn
35 40 45

Pro Asp Leu Gln Leu Pro Ser His Ile Gly Lys Gln Ala Trp Ser His
50 55 60

Ala Leu Gly Ser Leu
65

<210> 394

<211> 27
<212> PRT
<213> Homo sapiens

<400> 394
Met Ser Thr Tyr Ser His Thr Tyr Thr His Thr His Met His Ala His
1 5 10 15

Thr His Thr His Thr Leu Thr Leu Ser Leu Leu
20 25

<210> 395
<211> 23
<212> PRT
<213> Homo sapiens

<400> 395
Gly Ala Glu Gly Asp Arg His Leu Glu Gly Arg Ser Leu Ser Leu Arg
1 5 10 15

His Leu Gln Gly Ala Glu Thr
20

<210> 396
<211> 133
<212> PRT
<213> Homo sapiens

<400> 396
Val Val Glu Pro Gly Leu Lys Ala Ser Leu Gly Ala Met Ser Thr Leu
1 5 10 15

Phe Pro Ser Leu Phe Pro Arg Val Thr Glu Thr Leu Trp Phe Asn Leu
20 25 30

Asp Arg Pro Cys Val Glu Glu Thr Glu Leu Gln Gln Gln Glu Gln Gln
35 40 45

His Gln Ala Trp Leu Gln Ser Ile Ala Glu Lys Asp Asn Asn Leu Val
50 55 60

Pro Ile Gly Lys Pro Ala Ser Glu His Tyr Asp Asp Glu Glu Glu Glu
65 70 75 80

Asp Asp Glu Asp Asp Glu Asp Ser Glu Glu Asp Ser Glu Asp Asp Glu
85 90 95

Asp Met Gln Asp Met Asp Glu Met Asn Asp Tyr Asn Glu Ser Pro Asp
100 105 110

Asp Gly Glu Val Asn Glu Val Asp Met Glu Gly Asn Glu Gln Asp Gln
115 120 125

Asp Gln Trp Met Ile
130

<210> 397
<211> 23
<212> PRT
<213> Homo sapiens

<400> 397
Leu Phe Pro Arg Val Thr Glu Thr Leu Trp Phe Asn Leu Asp Arg Pro
1 5 10 15

Cys Val Glu Glu Thr Glu Leu
20

<210> 398
<211> 23
<212> PRT
<213> Homo sapiens

<400> 398
Tyr Asn Glu Ser Pro Asp Asp Gly Glu Val Asn Glu Val Asp Met Glu
1 5 10 15

Gly Asn Glu Gln Asp Gln Asp
20

<210> 399
<211> 101
<212> PRT
<213> Homo sapiens

<400> 399
Met Gly Phe Asp Ile His Gly Val Leu Gly Glu Ala Val Ala Glu Pro
1 5 10 15

Arg Glu Lys Lys Gln Glu Arg Ala Lys Trp Ala Pro His Asp Tyr Asp
20 25 30

Asp Pro Ser Leu Ser Leu Gln Asp Leu Leu Ile Ser Trp Met Ile Ser
35 40 45

Thr Trp Leu Ile Pro Met Trp Lys Cys Gln Ala Thr Ile Trp Phe Ser
50 55 60

Leu Ile Gln Arg Leu Leu Asn Ala Tyr Cys Met Pro Gly Asn Phe Arg
65 70 75 80

His Trp Glu Ile Ala Ala Asn Thr Thr Asn Lys Thr Pro Gly Leu Met
85 90 95

Asp Phe Lys Phe Leu
100

<210> 400
<211> 27
<212> PRT

<213> Homo sapiens

<400> 400
Glu Pro Arg Glu Lys Lys Gln Glu Arg Ala Lys Trp Ala Pro His Asp
1 5 10 15

Tyr Asp Asp Pro Ser Leu Ser Leu Gln Asp Leu
20 25

<210> 401
<211> 24
<212> PRT
<213> Homo sapiens

<400> 401
Met Pro Gly Asn Phe Arg His Trp Glu Ile Ala Ala Asn Thr Thr Asn
1 5 10 15

Lys Thr Pro Gly Leu Met Asp Phe
20

<210> 402
<211> 100
<212> PRT
<213> Homo sapiens

<400> 402
Gln Ser Val Pro Ser Pro Pro Leu Ala Pro Pro Leu Pro Pro Ser Leu
1 5 10 15

Pro Ser Phe Leu Phe Thr Glu Thr Arg Ser His Tyr Val Ala Arg Leu
20 25 30

Val Ser Asn Ser Trp Ala Gln Met Ile Leu Leu Pro Trp Pro Leu Lys
35 40 45

Val Leu Gly Leu Asp Val Ser His Cys Ala Trp Pro Lys Ser Val Phe
50 55 60

Leu Gln Ala Met Glu Glu Ile Ala Asp Phe Cys Leu Phe Ser Val Lys
65 70 75 80

Tyr Gln Val Ser Ser Met Thr Cys Phe Asp Arg Thr Ser Tyr Met Lys
85 90 95

Asn Thr Tyr Leu
100

<210> 403
<211> 27
<212> PRT
<213> Homo sapiens

<400> 403
Leu Phe Thr Glu Thr Arg Ser His Tyr Val Ala Arg Leu Val Ser Asn

1 5 10 15

Ser Trp Ala Gln Met Ile Leu Leu Pro Trp Pro
20 25

<210> 404
<211> 159
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (124)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (142)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 404
Ser Gln Ile Lys Ser Glu Lys Lys His Ile Gly Lys Ala Tyr Thr Cys
1 5 10 15

Thr Gln Thr Gln Ser Thr Gly Met Gln Ser Thr Leu Thr Ile Val Ala
20 25 30

Lys Lys Lys Ser Arg Asn His Thr Glu Ser Tyr Thr Arg Lys Lys Gln
35 40 45

Glu Asn Gln Ile Val Leu Ile Pro Trp His Gln Lys Lys His Pro Glu
50 55 60

Gly Thr His Thr Cys Ser His Ser Leu Arg Arg Asp Thr Asn Thr Ala
65 70 75 80

Ala Asp Thr Gln Arg Lys Ile Arg Ala His Arg Tyr Thr Tyr Arg Arg
85 90 95

Asp Lys Tyr Ser Asp Thr Leu Val Thr His Asp His Tyr Lys Gly Asp
100 105 110

Lys His Pro Ser Asn Thr His Thr Gln Pro Arg Xaa Glu Phe Leu Gln
115 120 125

Pro Gly Gly Ser Thr Asn Ser Arg Ala Ala Ala Pro Arg Xaa Ser Ser
130 135 140

Ser Phe Cys Pro Phe Ser Glu Gly Tyr Ser Ser Trp Gly Tyr His
145 150 155

<210> 405
<211> 26
<212> PRT
<213> Homo sapiens

<400> 405
Gly Met Gln Ser Thr Leu Thr Ile Val Ala Lys Lys Lys Ser Arg Asn
1 5 10 15

His Thr Glu Ser Tyr Thr Arg Lys Lys Gln
20 25

<210> 406
<211> 24
<212> PRT
<213> Homo sapiens

<400> 406
Lys Lys His Pro Glu Gly Thr His Thr Cys Ser His Ser Leu Arg Arg
1 5 10 15

Asp Thr Asn Thr Ala Ala Asp Thr
20

<210> 407
<211> 24
<212> PRT
<213> Homo sapiens

<400> 407
Arg Arg Asp Lys Tyr Ser Asp Thr Leu Val Thr His Asp His Tyr Lys
1 5 10 15

Gly Asp Lys His Pro Ser Asn Thr
20

<210> 408
<211> 91
<212> PRT
<213> Homo sapiens

<400> 408
Lys His Leu Pro Leu Lys Ala Pro Ile Asp Leu Asp Asn Lys Asn Ser
1 5 10 15

Cys Met Phe Cys Ser Arg Asp Ile Phe Cys Arg Phe His His Ser Thr
20 25 30

Ala Trp Leu Phe Leu Gly Arg Ile Thr Asp Arg Ile Leu Gly Leu His
35 40 45

His Tyr Leu Ile Arg Tyr Gln Phe Glu Ile Glu Asn Leu Cys Leu Met
50 55 60

Lys Ile Val Ile Pro Val Val Ser Met Lys Thr Asn Cys Gln Phe Asp
65 70 75 80

Phe Leu Gly Gln Leu Lys Gln Asn Leu Tyr His
85 90

<210> 409
<211> 28
<212> PRT
<213> Homo sapiens

<400> 409
Ile Glu Asn Leu Cys Leu Met Lys Ile Val Ile Pro Val Val Ser Met
1 5 10 15

Lys Thr Asn Cys Gln Phe Asp Phe Leu Gly Gln Leu
20 25

<210> 410
<211> 21
<212> PRT
<213> Homo sapiens

<400> 410
Ala Pro Ile Asp Leu Asp Asn Lys Asn Ser Cys Met Phe Cys Ser Arg
1 5 10 15

Asp Ile Phe Cys Arg
20

<210> 411
<211> 53
<212> PRT
<213> Homo sapiens

<400> 411
Gly Thr Ser Val Asn Glu Ser Val Ser Asn Ala Thr Ala Ile Asp Ser
1 5 10 15

Gln Ile Ala Arg Ser Leu His Ile Pro Leu Thr Gln Asp Ile Ala Gly
20 25 30

Asp Pro Ser Tyr Glu Ile Ser Lys Gln Arg Leu Ser Ile Val Ile Gly
35 40 45

Val Val Ala Gly Ile
50

<210> 412
<211> 220
<212> PRT
<213> Homo sapiens

<400> 412
Pro Lys Ile Lys Met Ala Met Lys Pro Ala Lys Lys Ile Thr Lys Thr
1 5 10 15

Phe Leu His Pro Asn Ser Met Thr Asn Leu Lys Ser Leu Lys Arg Thr
20 25 30

Arg Lys Thr Lys Asn Leu Ser Ser Leu Ser Thr Ala Ala Leu Ser Leu
35 40 45

Trp Arg Leu Leu Ser Gln Met Asp Arg Gly Met Ile Val Ser Met Arg
50 55 60

Ser Cys Gln Thr Ala Gln Ala Trp Gly Asp Thr Gly Pro Leu Met Val
65 70 75 80

Gly Pro Ala Val Leu Thr Trp Gln Gly Ile Thr Asn Leu Val Pro His
85 90 95

Cys Leu Leu Phe Ser Phe Ile Pro Ser His Gln Leu Gln Glu Lys Asn
100 105 110

Thr Arg Pro Tyr Lys Ile Tyr His Gln Pro Thr His Leu Trp Glu Gln
115 120 125

Glu Thr Thr Phe Gln Leu Asp Gln Ile Thr Ala Leu Ser Thr Ala Val
130 135 140

Lys Pro Ile Thr Ser Thr Ala Asn Arg Cys Val Tyr Ile His Thr Leu
145 150 155 160

Leu Cys Leu Ala Glu Phe His Ser Asn Met Met Leu His Tyr Ala Pro
165 170 175

Tyr Cys Asp Asp Leu Ser Thr Pro Lys Pro Ala Gly Ala Cys Pro Trp
180 185 190

Pro Trp Gly Val Ser Gln Ser Leu Leu Val Pro Leu Val Val His Phe
195 200 205

Ile Phe Glu Ser Phe Ser Phe Ser Tyr Thr Glu Lys
210 215 220

<210> 413
<211> 55
<212> PRT
<213> Homo sapiens

<400> 413
Cys Ser Ile Met His His Thr Val Met Thr Phe Leu Leu Arg Asn Leu
1 5 10 15

Leu Glu Pro Ala Leu Gly Arg Gly Val Ser Ala Asn His Cys Leu Phe
20 25 30

His Leu Leu Tyr Ile Leu Phe Leu Ser Leu Phe Leu Ser His Ile Gln
35 40 45

Lys Asn Ser Met Lys Ile Lys
50 55

<210> 414
<211> 29

<212> PRT
<213> Homo sapiens

<400> 414
Thr Ala Ile Asp Ser Gln Ile Ala Arg Ser Leu His Ile Pro Leu Thr
1 5 10 15

Gln Asp Ile Ala Gly Asp Pro Ser Tyr Glu Ile Ser Lys
20 25

<210> 415
<211> 21
<212> PRT
<213> Homo sapiens

<400> 415
Tyr Cys Arg Ser Lys Asn Lys Asn Gly Tyr Glu Ala Gly Lys Lys Asp
1 5 10 15

His Glu Asp Phe Phe
20

<210> 416
<211> 21
<212> PRT
<213> Homo sapiens

<400> 416
Gly Pro Gly Ser Pro Asp Leu Ala Arg His Tyr Lys Ser Ser Ser Pro
1 5 10 15

Leu Pro Thr Val Gln
20

<210> 417
<211> 25
<212> PRT
<213> Homo sapiens

<400> 417
Leu Pro Pro Ala Asn Thr Phe Val Gly Ala Gly Asp Asn Ile Ser Ile
1 5 10 15

Gly Ser Asp His Cys Ser Glu Tyr Ser
20 25

<210> 418
<211> 119
<212> PRT
<213> Homo sapiens

<400> 418
Gly Thr Ser Asn Ala Ser Val Ser Pro Thr Ile Cys Ile Cys Met Cys
1 5 10 15

Gly Tyr Val His Ile Trp Phe Phe Ile Cys Leu Cys Val Tyr Leu Lys
20 25 30

Val Leu Gln Gly Ser Ala Cys Pro Trp Ile Ala Ala Ala Val Val Met
35 40 45

Arg Arg Met Arg Lys Val Gln Glu Lys Gly Glu Val Phe Arg Asn Met
50 55 60

Ala Ala Thr Trp Ala Leu Arg Ser Gly Ile Gln Ser Leu Asn Ser Leu
65 70 75 80

Val Ser Ser Ala Phe Phe Thr Ile Phe Met Thr Leu Gly Ser Ser Trp
85 90 95

Asn Leu Ile Val Ser Leu Ser Ser Leu Val Asn Trp Thr Gly Leu Phe
100 105 110

Ser Phe Tyr Phe Ser Arg Asn
115

<210> 419
<211> 28
<212> PRT
<213> Homo sapiens

<400> 419
Cys Leu Cys Val Tyr Leu Lys Val Leu Gln Gly Ser Ala Cys Pro Trp
1 5 10 15

Ile Ala Ala Ala Val Val Met Arg Arg Met Arg Lys
20 25

<210> 420
<211> 26
<212> PRT
<213> Homo sapiens

<400> 420
Thr Ile Phe Met Thr Leu Gly Ser Ser Trp Asn Leu Ile Val Ser Leu
1 5 10 15

Ser Ser Leu Val Asn Trp Thr Gly Leu Phe
20 25

<210> 421
<211> 58
<212> PRT
<213> Homo sapiens

<400> 421
Gln Pro Asp Ile Pro Val Leu Pro Val Gly Phe Ser Gln Asn Cys Ser
1 5 10 15

```
Phe Lys Val Ser Gly Cys Trp Lys Gly Gly Leu Ile Ala Glu Lys Val
            20                  25                  30

Gly Thr Leu Gly Thr Pro Lys Gly Arg Arg Ala Trp Pro Glu Thr Glu
        35                  40                  45

Phe Phe Arg Phe Leu Glu Pro Gly Leu Pro
    50                  55
```

<210> 422
<211> 131
<212> PRT
<213> Homo sapiens

<400> 422

```
Arg Gly Phe Arg Met Ala Gln Pro Leu Val Asn Thr Phe Gln Val Ala
 1               5                  10                  15

Val Pro Val Glu Asp Leu Ala Pro Gln Gln Asn Pro Ser Arg Phe Pro
            20                  25                  30

Ala Asp Pro Ala Leu Leu Ser Phe Leu Thr Gly Ser Ile Leu Ala Pro
        35                  40                  45

Gly Lys Val Ile Trp Val Asn Val Ser Phe Thr Ala Ile Ile Trp Pro
    50                  55                  60

Thr Trp Asp Ser Met Ala Ile Gly Glu Leu Thr Ile Ala Ser His Ala
65                  70                  75                  80

Ser Met Thr Leu His Ile Gly Arg Pro Gly Ser Arg Lys Arg Lys Asn
                85                  90                  95

Ser Val Ser Gly His Ala Arg Leu Pro Phe Gly Val Pro Ser Val Pro
            100                 105                 110

Thr Phe Ser Ala Ile Ser Pro Pro Phe Gln Gln Pro Glu Thr Leu Lys
        115                 120                 125

Glu Gln Phe
    130
```

<210> 423
<211> 24
<212> PRT
<213> Homo sapiens

<400> 423

```
Glu Asp Leu Ala Pro Gln Gln Asn Pro Ser Arg Phe Pro Ala Asp Pro
 1               5                  10                  15

Ala Leu Leu Ser Phe Leu Thr Gly
            20
```

<210> 424

<211> 29
<212> PRT
<213> Homo sapiens

<400> 424

```
Thr Trp Asp Ser Met Ala Ile Gly Glu Leu Thr Ile Ala Ser His Ala
 1               5                  10                  15

Ser Met Thr Leu His Ile Gly Arg Pro Gly Ser Arg Lys
            20                  25
```

<210> 425
<211> 71
<212> PRT
<213> Homo sapiens

<400> 425

```
Val Ser Pro Gln Leu Met Gly Ile Lys Arg Glu Pro Ser Ala Ala Gln
 1               5                  10                  15

Leu Ser Val Gly Glu Glu His Thr Leu Asp Arg Glu Gly Arg Glu Leu
            20                  25                  30

Val Asp Leu Pro Gly Gln Pro Ser Gln Lys Ile Lys Ile Lys Asn Lys
        35                  40                  45

Ser Ser Leu His Pro Gly Leu Ile Ile Pro Pro Ala His Tyr Lys Thr
    50                  55                  60

Ala Thr Thr Thr Asn Leu Phe
65                  70
```

<210> 426
<211> 21
<212> PRT
<213> Homo sapiens

<400> 426

```
Pro Ser Ala Ala Gln Leu Ser Val Gly Glu Glu His Thr Leu Asp Arg
 1               5                  10                  15

Glu Gly Arg Glu Leu
            20
```

<210> 427
<211> 23
<212> PRT
<213> Homo sapiens

<400> 427

```
Asn Cys Asp His Asp Phe Ile Gln Pro Leu His Thr Pro Met Ser Ala
 1               5                  10                  15

Leu Phe Gln Ser Glu Phe Ser
            20
```

<210> 428
<211> 107
<212> PRT
<213> Homo sapiens

<400> 428
Ser Ile Leu Asn Met Gly Leu Phe Thr Glu Gln Arg Pro Trp Pro Ala
1 5 10 15

Ala Ala Arg Cys Ala Arg Gln Ser Thr Val Ala Gly Ala Ile Arg Arg
20 25 30

Ala Arg Gly Thr Val Thr Met Trp Gln Val Ala Gly Ala Ala Trp Ala
35 40 45

Ser Pro Asp Arg Arg Ala Lys Val His Pro Cys Arg His Ala Ala Pro
50 55 60

Cys Leu Pro Ser Pro Cys Arg Arg Gly Leu Gln Met Ser Gly Pro Leu
65 70 75 80

Gln Ala Thr Arg Gly Arg Val Thr Leu Arg Ser His Gln Val Gly Cys
85 90 95

Lys Arg Ala Thr Gly Ser Ile Glu Asn Ser Leu
100 105

<210> 429
<211> 114
<212> PRT
<213> Homo sapiens

<400> 429
Gln Lys Ser Lys Gly Ser Pro Leu Gln Thr Cys Cys Ser Leu Pro Thr
1 5 10 15

Leu Pro Met Gln Glu Arg Pro Ala Asp Glu Trp Ser Thr Pro Gly Asp
20 25 30

Gln Gly Lys Ser Tyr Ile Lys Lys Pro Pro Gly Gly Leu Gln Lys Gly
35 40 45

His Arg Leu His Arg Lys Leu Thr Leu Lys Gln Gly Arg His Arg Gly
50 55 60

Val Glu Gly Leu Asn Glu Ile Met Val Thr Val Leu Lys Glu Glu Phe
65 70 75 80

Pro Val Ser Lys Pro Gly Leu Asn Val Leu Pro Thr Phe His Arg His
85 90 95

His Glu Cys Tyr Gln His Gly Met Asn Leu Thr Ala Arg Ile Ser Val
100 105 110

Val Ser

<210> 430
<211> 25
<212> PRT
<213> Homo sapiens

<400> 430
Ala Arg Gln Ser Thr Val Ala Gly Ala Ile Arg Arg Ala Arg Gly Thr
1 5 10 15

Val Thr Met Trp Gln Val Ala Gly Ala
20 25

<210> 431
<211> 25
<212> PRT
<213> Homo sapiens

<400> 431
Pro Cys Arg Arg Gly Leu Gln Met Ser Gly Pro Leu Gln Ala Thr Arg
1 5 10 15

Gly Arg Val Thr Leu Arg Ser His Gln
20 25

<210> 432
<211> 26
<212> PRT
<213> Homo sapiens

<400> 432
Leu Pro Met Gln Glu Arg Pro Ala Asp Glu Trp Ser Thr Pro Gly Asp
1 5 10 15

Gln Gly Lys Ser Tyr Ile Lys Lys Pro Pro
20 25

<210> 433
<211> 23
<212> PRT
<213> Homo sapiens

<400> 433
Asn Val Leu Pro Thr Phe His Arg His His Glu Cys Tyr Gln His Gly
1 5 10 15

Met Asn Leu Thr Ala Arg Ile
20

<210> 434
<211> 40
<212> PRT

<213> Homo sapiens

<400> 434
Ile Asn Val Leu Tyr Cys Ser Arg Asp Ser Leu Met Gly Arg Thr Ile
1 5 10 15

Met Glu Ser Ser Asp Tyr Ile Lys Lys Gly Ala Asn Val Ser Pro Val
20 25 30

Leu Gly Val Arg Gln Gln Ala Val
35 40

<210> 435
<211> 28
<212> PRT
<213> Homo sapiens

<400> 435
Ser Leu Leu Met Tyr Phe Val Phe Lys Ile Phe Phe Gln Ser Leu Cys
1 5 10 15

Val Leu Gly Tyr Cys Ile Leu Pro Leu Thr Val Ala
20 25

<210> 436
<211> 50
<212> PRT
<213> Homo sapiens

<400> 436
Arg Leu Trp Met Thr Lys Ala His Pro Ala Leu Arg His Leu Leu Leu
1 5 10 15

Leu Phe Thr Leu Ala Leu Thr Leu Leu Ala Gln Gly Cys Cys Ala Val
20 25 30

Ala Pro Ser Gly Cys Ala Asp Leu Ala Gly Phe Cys Ser Leu Gly His
35 40 45

Ser Cys
50

<210> 437
<211> 48
<212> PRT
<213> Homo sapiens

<400> 437
Arg Thr Cys Thr Pro Trp Met Gly Phe Trp Cys Leu Val Cys Ser Leu
1 5 10 15

Phe Ala Pro Val Pro Thr Ser Arg Lys Tyr Leu Val Ser Lys Pro Gly
20 25 30

Cys Tyr Gln Arg Arg Arg Val Phe Gly Val Cys Phe Thr Lys Pro Leu

35 40 45

<210> 438
<211> 8
<212> PRT
<213> Homo sapiens

<400> 438
Trp Leu Leu Ser Glu Lys Lys Gly
1 5

<210> 439
<211> 10
<212> PRT
<213> Homo sapiens

<400> 439
Gly Val Phe Tyr Lys Ala Ala Val Ile Gly
1 5 10

<210> 440
<211> 45
<212> PRT
<213> Homo sapiens

<400> 440
Cys Lys Thr Ser Pro Leu Pro Lys Glu Gly Gln Ser Ala Val Ser Val
1 5 10 15

Pro Val Ser Ser His Phe Leu Ala His Ser Ala Pro Leu Ser Gly Gly
20 25 30

His Ala His Val Phe Ala Arg Asp Gly Ala Thr Gly Leu
35 40 45

<210> 441
<211> 140
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (54)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 441
Leu Gly Arg Gly Ser Gly Glu Arg Lys Thr Pro Val Ser Cys Phe Ala
1 5 10 15

Gln Ile Ser Lys Ser Arg Gly Gly Arg Ser Lys Ser Leu Thr His Leu
20 25 30

```
Cys Thr His Thr His Thr Gln Val Thr Glu Leu Asp Val Arg Met Ser
      35                  40                  45

His Gly Cys Leu Arg Xaa Gln His Ala Gly Arg Leu Ala Pro Pro Pro
     50                  55                  60

Pro Leu Arg Phe Cys Leu Thr Ala Cys Trp Gly Arg Arg Gly Glu Ala
 65                  70                  75                  80

Glu Thr Val Trp Lys Asp Pro Ala Ser Ser Gln His Pro Pro Pro Ser
                 85                  90                  95

Glu Lys Pro His Arg Gln Asp Arg His Pro Glu Arg Trp His Gln Pro
            100                 105                 110

Gly Gly Pro Ile Pro Gly Lys His Met Arg Val Ser Pro Gly Gln Arg
        115                 120                 125

Gly Arg Val Cys Gln Glu Met Gly Arg Asn Arg Asn
    130                 135                 140


<210> 442
<211> 102
<212> PRT
<213> Homo sapiens

<400> 442
Phe Cys Leu Arg Asp Phe Lys Ile Trp Arg Gly Arg Leu Glu Ala Gly
  1               5                  10                  15

Arg Thr Glu Gly Arg Leu Ala Gly Glu Arg Phe Gly Gly Glu Glu Asp
             20                  25                  30

Pro Ser Phe Leu Phe Cys Ser Asp Phe Lys Val Glu Gly Trp Ala Phe
         35                  40                  45

Glu Ile Ser His Ser Leu Val His Thr His Thr His Thr Gly His Gly
     50                  55                  60

Ala Gly Arg Ala Asp Val Thr Arg Val Pro Ala Gly Thr Ala Arg Trp
 65                  70                  75                  80

Glu Ala Gly Ser Pro Thr Pro Ser Pro Val Leu Phe Asp Ser Leu Leu
                 85                  90                  95

Gly Ala Ala Gly Arg Gly
            100


<210> 443
<211> 28
<212> PRT
<213> Homo sapiens

<400> 443
Ala Gln Ile Ser Lys Ser Arg Gly Gly Arg Ser Lys Ser Leu Thr His
```



```
  1               5                  10                  15

Leu Cys Thr His Thr His Thr Gln Val Thr Glu Leu
            20                  25


<210> 444
<211> 26
<212> PRT
<213> Homo sapiens

<400> 444
Glu Lys Pro His Arg Gln Asp Arg His Pro Glu Arg Trp His Gln Pro
  1               5                  10                  15

Gly Gly Pro Ile Pro Gly Lys His Met Arg
            20                  25


<210> 445
<211> 26
<212> PRT
<213> Homo sapiens

<400> 445
Gly Arg Leu Glu Ala Gly Arg Thr Glu Gly Arg Leu Ala Gly Glu Arg
  1               5                  10                  15

Phe Gly Gly Glu Glu Asp Pro Ser Phe Leu
            20                  25


<210> 446
<211> 23
<212> PRT
<213> Homo sapiens

<400> 446
Val Thr Arg Val Pro Ala Gly Thr Ala Arg Trp Glu Ala Gly Ser Pro
  1               5                  10                  15

Thr Pro Ser Pro Val Leu Phe
            20


<210> 447
<211> 31
<212> PRT
<213> Homo sapiens

<400> 447
Asp Glu Gly Val Gln Gly Glu Arg Leu Phe Arg Ile Leu Arg Ile Asn
  1               5                  10                  15

Gly Glu Lys Pro Tyr Asn Phe Val Asp Tyr Phe His Cys Glu Tyr
            20                  25                  30
```

<210> 448
<211> 111
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (59)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (62)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (65)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (66)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 448
Lys Val Val Arg Ile Asp Asn Gly Ile Leu Cys Ser His Lys Lys Thr
1 5 10 15

Glu Ile Met Ser Leu Gln Gln His Gly Trp Ile Trp Arg Pro Tyr Leu
20 25 30

Lys Gln Thr Asn Thr Gly Thr Glu Asn Gln Ile Pro His Thr Leu Thr
35 40 45

Tyr Lys Trp Glu Leu Asn Phe Glu Tyr Ile Xaa Thr Gln Xaa Arg Gly
50 55 60

Xaa Xaa Asp Ser Glu Ala Tyr Leu Lys Val Glu Gly Gly Arg Arg Glu
65 70 75 80

Gly Ile Gln Lys Leu Pro Ile Arg Tyr Tyr Val Tyr Tyr Leu Gly Asp
85 90 95

Lys Ile Ile Cys Thr Ser Ser Ser Cys Ser Met His Leu Leu Met
100 105 110

<210> 449
<211> 21
<212> PRT
<213> Homo sapiens

<400> 449
His Lys Asp Thr Cys Met Ser Met Phe Thr Ala Ala Leu Phe Thr Ile
1 5 10 15

Ala Lys Thr Trp Asn

20

<210> 450
<211> 14
<212> PRT
<213> Homo sapiens

<400> 450
Met Pro Ile Asn Asp Arg Leu Asp Phe Lys Arg Trp Tyr Val
1 5 10

<210> 451
<211> 47
<212> PRT
<213> Homo sapiens

<400> 451
Thr Met Glu Ser Tyr Val Ala Ile Lys Arg Gln Arg Ser Cys Pro Cys
1 5 10 15

Ser Asn Met Val Gly Ser Gly Gly His Ile Leu Ser Lys Leu Thr Gln
20 25 30

Glu Gln Lys Thr Lys Tyr His Ile Leu Ser Leu Ile Ser Gly Ser
35 40 45

<210> 452
<211> 25
<212> PRT
<213> Homo sapiens

<400> 452
Glu Ile Met Ser Leu Gln Gln His Gly Trp Ile Trp Arg Pro Tyr Leu
1 5 10 15

Lys Gln Thr Asn Thr Gly Thr Glu Asn
20 25

<210> 453
<211> 24
<212> PRT
<213> Homo sapiens

<400> 453
Arg Arg Glu Gly Ile Gln Lys Leu Pro Ile Arg Tyr Tyr Val Tyr Tyr
1 5 10 15

Leu Gly Asp Lys Ile Ile Cys Thr
20

<210> 454
<211> 57
<212> PRT

<213> Homo sapiens

<400> 454
Leu His Gly Glu Gln Val Pro Ile Tyr Ile Phe Leu Leu Met Gln Pro
1 5 10 15

Leu Asn Phe Glu Cys Ile Ser Phe Leu Asn Cys Ile Glu Gln Tyr Ser
20 25 30

Val Gly Val Ile His Asn Ser Val Thr Ile Tyr Ala Cys Asp Arg Glu
35 40 45

Glu Asn Cys Met Asp Ile Arg Tyr Leu
50 55

<210> 455
<211> 12
<212> PRT
<213> Homo sapiens

<400> 455
Gly Thr Ser Trp Ala Ser Arg Phe Phe Thr Cys His
1 5 10

<210> 456
<211> 52
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (5)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (7)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (15)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (18)
<223> Xaa equals any of the naturally occurring L-amino acids

<220>
<221> SITE
<222> (37)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 456
Gly Pro Pro Arg Xaa Phe Xaa Pro Lys Lys Ala Ile Leu Gly Xaa Pro

1 5 10 15

Pro Xaa Gly Arg Val Pro Pro Phe Arg Tyr Arg Ser Arg Asn Ser Arg
20 25 30

Gly Arg Pro His Xaa Ser Ala Pro Arg Val Arg Phe Cys Leu Glu Asn
35 40 45

Ser Trp Leu Arg
50

<210> 457
<211> 72
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (56)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 457
Pro Leu Asn Thr Met Met Cys Met Met Cys Lys Met Lys Val Ser Pro
1 5 10 15

Lys Ile Phe Ser Lys Leu Lys Arg Lys Tyr Leu Asn Ser Asn Thr Leu
20 25 30

Thr Lys Leu Glu Met Gln Thr Val His Leu Glu Ser Ser Leu Ala Ser
35 40 45

Cys Ser Pro Asn Lys Ser Gly Xaa Val Gly Arg Thr Arg Gly Val Asp
50 55 60

Pro Gly Asn Ser Gly Thr Gly Thr
65 70

<210> 458
<211> 69
<212> PRT
<213> Homo sapiens

<400> 458
Gly Thr Val Thr Gln Lys Arg Lys Cys Val Phe Gly Lys Tyr Leu Leu
1 5 10 15

Ser Thr Cys Ser Leu Met Phe Ser Ser Met His Gly Ala Cys Ser Trp
20 25 30

Lys Ala Lys Gln Thr Ser Ser Ser Ala Gly Phe Leu Cys Leu His Val
35 40 45

Leu Cys Pro Ala Leu Gln Leu Thr Arg Glu Lys Tyr Lys Thr Trp Pro
50 55 60

Trp Pro Ser Phe Ile

65

<210> 459
<211> 69
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (21)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 459
Met Lys Glu Gly Gln Gly His Val Leu Tyr Phe Ser Arg Val Asn Cys
1 5 10 15

Lys Ala Gly His Xaa Thr Cys Arg Gln Arg Lys Pro Ala Asp Glu Leu
20 25 30

Val Cys Phe Ala Phe Gln Glu Gln Ala Pro Cys Ile Leu Leu Asn Ile
35 40 45

Arg Leu Gln Val Leu Asn Lys Tyr Leu Pro Asn Thr His Phe Leu Phe
50 55 60

Cys Val Thr Val Pro
65

<210> 460
<211> 69
<212> PRT
<213> Homo sapiens

<400> 460
Thr Met Thr Gly Ile Asp Ser Ser Pro Glu Glu Ile Leu Arg Gln Val
1 5 10 15

Gly Cys Lys Gln Gln Gln Gly Lys Gly Val Glu His Val Glu Gly Ser
20 25 30

Ser Ala Glu Ala Gly Glu Ala Ala Arg Gly Gly Gly Ala Lys Gly Gly
35 40 45

Gly Gly Ala Ala Gly Lys Gly Thr Ser Lys Val Gly Thr Leu Arg Arg
50 55 60

Thr Arg Gly Ser Thr
65

<210> 461
<211> 185
<212> PRT
<213> Homo sapiens

<220>

<221> SITE
<222> (22)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 461
Ala Gln Arg Glu Ala Gly Ser Arg Pro Arg Arg Arg Lys Ser Leu Lys
1 5 10 15

Ala Val Ala Met Leu Xaa Val Glu Met Gly Gly Gly Cys Arg Gly Ser
20 25 30

Met Gly Pro Gly Pro Gly Tyr Ser Ala Gly Ser Arg Val Cys Arg Gly
35 40 45

Ser Ser Leu Pro Gln Val Ala Pro Phe Asn Pro Ser Arg Ala His Leu
50 55 60

Leu Pro Pro Pro Val Gly Gly Gly Leu Asn Ser Val Trp Leu Ser Gly
65 70 75 80

Val Gln Leu Ser Thr Pro Pro Tyr Ala Asp Trp Glu Gly Val Gly Gln
85 90 95

Ser Pro Gln Pro Arg Gly Pro Trp Met Gly Ser Ser Ser Leu Gly Thr
100 105 110

Val Gly Pro Gly Cys Val Leu Ser Gly Cys Pro Thr Val Lys Ala Asn
115 120 125

Gly Gly Ser Pro Cys Ser Glu Met Leu Gly Glu Arg Arg Leu Leu Glu
130 135 140

Pro Ser Val Gly Pro Val Ser Gly Cys Pro Glu Arg Arg Glu Gly Gly
145 150 155 160

His Gly Ala Arg Gly Ala Ala Gly Val Val Val Lys Gly His Ala Ser
165 170 175

Val Gln Leu Asn Phe Leu Ser Leu Ile
180 185

<210> 462
<211> 102
<212> PRT
<213> Homo sapiens

<400> 462
Lys Ala Glu Phe Thr Phe Ala Lys Glu Lys Asn Ala Lys Ala Gln Leu
1 5 10 15

Gly Lys Lys Gly Thr Arg Trp Val Lys His Asp Lys Arg Lys Glu Ile
20 25 30

Gln Leu Tyr Gly Cys Val Thr Leu Asn Asp Asp Pro Ser Cys Pro Pro
35 40 45

Cys Pro Val Pro Thr Leu Pro Pro Phe Trp Thr Ala Thr Tyr Gly Ser

```
     50                  55                  60

His Gly Arg Phe Gln Lys Pro Pro Phe Ser Gln His Leu Arg Ala Gly
 65                  70                  75                  80

Gly Ala Pro Val Gly Leu Asp Cys Gly Ala Pro Thr Gln Tyr Ala Ala
                85                  90                  95

Arg Pro His Gly Pro Lys
            100


<210> 463
<211> 26
<212> PRT
<213> Homo sapiens

<400> 463
Gly Cys Arg Gly Ser Met Gly Pro Gly Pro Gly Tyr Ser Ala Gly Ser
  1               5                  10                  15

Arg Val Cys Arg Gly Ser Ser Leu Pro Gln
            20                  25


<210> 464
<211> 22
<212> PRT
<213> Homo sapiens

<400> 464
Gln Pro Arg Gly Pro Trp Met Gly Ser Ser Ser Leu Gly Thr Val Gly
  1               5                  10                  15

Pro Gly Cys Val Leu Ser
            20


<210> 465
<211> 21
<212> PRT
<213> Homo sapiens

<400> 465
Gly Ala Ala Gly Val Val Val Lys Gly His Ala Ser Val Gln Leu Asn
  1               5                  10                  15

Phe Leu Ser Leu Ile
            20


<210> 466
<211> 94
<212> PRT
<213> Homo sapiens

<400> 466
Gly Lys Pro Leu Ser Ala Ile Phe Pro Ile Cys His Met Met Phe Leu
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 1               5                  10                  15

Pro Gly Lys Phe Asn Leu Gly Ile Ser His Arg Cys Cys Arg Met Thr
            20                  25                  30

Ser Pro Trp Asp Lys Arg Gln Gln Leu Arg Gln Glu Cys Lys Ser Asp
        35                  40                  45

Pro His Val Gln Asn Pro Arg Ile His Phe Pro Glu Ser Lys Asn Ser
    50                  55                  60

Phe Pro Ser Ala Tyr Ile Phe Val Ser Glu Gly Asn Gly Val Ser Pro
65                  70                  75                  80

Ser Lys Trp His Cys Ile Tyr Ser Gly Thr Ser Leu Ser His
                85                  90


<210> 467
<211> 62
<212> PRT
<213> Homo sapiens

<400> 467
Gly Glu Arg Gly Arg Tyr Gln Ser Lys Tyr Ser Ala Thr Trp Met Val
  1               5                  10                  15

Thr Pro His Tyr Leu Gln Thr Gln Arg Cys Lys Leu Arg Glu Met Asn
            20                  25                  30

Ser Trp Ile Gln Gly Asn Glu Phe Leu Asp Ser Glu His Glu Gly Gln
        35                  40                  45

Ile Tyr Ile Pro Val Ser Ile Val Asp Ala Tyr Pro Lys Asp
    50                  55                  60


<210> 468
<211> 107
<212> PRT
<213> Homo sapiens

<400> 468
Ile Ser Ile Arg Gly Arg Ile Leu Tyr Lys Met Ala Tyr Phe Lys Val
  1               5                  10                  15

Cys Val Ile Ile Trp Phe Gln Gln Phe Cys Val Glu Glu Thr Ser Ile
            20                  25                  30

Ile Lys Asn Val Arg Met Leu Thr Ser Glu Phe Gln Asn Ser Tyr Ala
        35                  40                  45

Thr Pro Val Ser Gly Leu Leu Pro Gly Ala Val Ala Trp Arg Gly Gly
    50                  55                  60

Ala Val Tyr Gly Trp Val Arg His Ala Met Gln Val Leu Gln Lys Glu
65                  70                  75                  80
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Pro Thr Gln Pro Ser Ser Phe Leu Pro Pro Ser Asp Ala Ala Ser Phe
                85                  90                  95

Trp Gly Pro Glu Ser Arg Leu His Leu Thr Trp
            100                 105


<210> 469
<211> 86
<212> PRT
<213> Homo sapiens

<400> 469
Lys Pro Phe Ala Phe Ser Ala Arg Asn Phe Pro Thr Met Leu Ser Glu
  1               5                  10                  15

Ala Tyr Phe Gln Asp Pro Arg Met Arg Gln His His Leu Gly Val Glu
             20                  25                  30

Arg Met Thr Val Ala Trp Val Pro Ser Ala Ile Pro Ala Trp Arg Ala
         35                  40                  45

Ser Pro Thr Arg Thr Gln His His Pro Ser Lys Pro Gln His Gln Glu
     50                  55                  60

Gly Ala Gln Lys Gln Gly Trp His Met Asn Ser Gly Ile Leu Met Ser
 65                  70                  75                  80

Ala Tyr Glu His Phe Leu
                85


<210> 470
<211> 60
<212> PRT
<213> Homo sapiens

<400> 470
His Ser Lys Gln Asn Ile Cys Arg Glu Val Asn Ile Leu Lys Met Phe
  1               5                  10                  15

Leu His Glu Ile Lys Lys Thr Val Thr Asp Asn Ile Ser Thr Gln Arg
             20                  25                  30

Arg Phe Thr Tyr Asn His Gln Pro Gly Ser Val Ser Ile Phe Ser Val
         35                  40                  45

Thr Asp Ile Leu Asp Phe Glu Val Pro Phe Gly Leu
     50                  55                  60


<210> 471
<211> 57
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
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<222> (28)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 471
Lys Val Ile Asp Val Ile Phe Ser Leu Pro Pro Gly Arg Lys Ala Thr
  1               5                  10                  15

Phe Ser Cys Pro Leu Ala Pro Leu Ser Gly Ala Xaa Gly Leu Pro Gly
             20                  25                  30

Gly Gly Ala Asn Arg Pro Gly Pro Phe Leu Pro Cys Ile Gln Pro Trp
         35                  40                  45

Gly Pro Leu Arg Leu Pro Glu Gly Cys
     50                  55


<210> 472
<211> 80
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (25)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 472
Met Ser Ser Ser Leu Cys Pro Gln Gly Gly Lys Pro Pro Ser Leu Ala
  1               5                  10                  15

Pro Trp Pro Leu Cys Gln Gly Pro Xaa Val Cys Arg Val Gly Val Pro
             20                  25                  30

Thr Gly Leu Ala Leu Ser Ser Pro Ala Ser Ser His Gly Gly Leu Cys
         35                  40                  45

Asp Cys Arg Lys Val Ala Trp Leu Val Pro Gly Pro Ala Gln Ala Arg
     50                  55                  60

Gly Arg Ala Ala Trp Phe Tyr Phe Tyr Leu Thr Leu Phe Ser Val Leu
 65                  70                  75                  80


<210> 473
<211> 26
<212> PRT
<213> Homo sapiens

<400> 473
Leu Ala Leu Ser Ser Pro Ala Ser Ser His Gly Gly Leu Cys Asp Cys
  1               5                  10                  15

Arg Lys Val Ala Trp Leu Val Pro Gly Pro
             20                  25
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<210> 474
<211> 160
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (124)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 474
Met Gln Arg Glu Arg Trp Ala Arg Pro Trp Met Ala Ser Thr Val Glu
1 5 10 15

Ser Arg Met Pro Glu Gly Lys Trp Arg Arg Phe Ser Thr Asp Leu Ala
20 25 30

Thr Trp Gly Ala Thr Pro Ala Arg Ser Trp Thr Lys Ala Ser Arg Gly
35 40 45

Ser Thr Thr Ala Trp Thr Arg Leu Pro Met Arg Ser Thr Met Val Leu
50 55 60

Asp Lys Gln Glu Arg Lys Gln Arg Ser Leu Ala Met Gly Ser Thr Thr
65 70 75 80

Leu Leu Asp Arg Pro Gly Arg Lys Gln Thr Lys Arg Ser Lys Gly Ser
85 90 95

Thr Leu Gly Ser Thr Arg Leu Gly Arg Lys Gln Arg Asn Leu Ala Lys
100 105 110

Gly Ser Thr Met Leu Leu Thr Arg Leu Glu Arg Xaa Trp Arg Ser Leu
115 120 125

Ala Gln Val Pro Thr Met Leu Leu Ala Arg Pro Gly Arg Ser Cys Arg
130 135 140

Met Leu Ile Met Gly Ser Thr Lys Pro Ala Arg Arg Pro Thr Ser Cys
145 150 155 160

<210> 475
<211> 264
<212> PRT
<213> Homo sapiens

<400> 475
Met Arg Pro Leu Leu Gly Leu Leu Leu Val Phe Ala Gly Cys Thr Phe
1 5 10 15

Ala Leu Tyr Leu Leu Ser Thr Arg Leu Pro Arg Gly Arg Arg Leu Gly
20 25 30

Ser Thr Glu Glu Ala Gly Gly Arg Ser Leu Trp Phe Pro Ser Asp Leu
35 40 45

Ala Glu Leu Arg Glu Leu Ser Glu Val Leu Arg Glu Tyr Arg Lys Glu
50 55 60

His Gln Ala Tyr Val Phe Leu Leu Phe Cys Gly Ala Tyr Leu Tyr Lys
65 70 75 80

Gln Gly Phe Ala Ile Pro Gly Ser Ser Phe Leu Asn Val Leu Ala Gly
85 90 95

Ala Leu Phe Gly Pro Trp Leu Gly Leu Leu Leu Cys Cys Val Leu Thr
100 105 110

Ser Val Gly Ala Thr Cys Cys Tyr Leu Leu Ser Ser Ile Phe Gly Lys
115 120 125

Gln Leu Val Val Ser Tyr Phe Pro Asp Lys Val Ala Leu Leu Gln Arg
130 135 140

Lys Val Glu Glu Asn Arg Asn Ser Leu Phe Phe Phe Leu Leu Phe Leu
145 150 155 160

Arg Leu Phe Pro Met Thr Pro Asn Trp Phe Leu Asn Leu Ser Ala Pro
165 170 175

Ile Leu Asn Ile Pro Ile Val Gln Phe Phe Phe Ser Val Leu Ile Gly
180 185 190

Leu Ile Pro Tyr Asn Phe Ile Cys Val Gln Thr Gly Ser Ile Leu Ser
195 200 205

Thr Leu Thr Ser Leu Asp Ala Leu Phe Ser Trp Asp Thr Val Phe Lys
210 215 220

Leu Leu Ala Ile Ala Met Val Ala Leu Ile Pro Gly Thr Leu Ile Lys
225 230 235 240

Lys Phe Ser Gln Lys His Leu Gln Leu Asn Glu Thr Ser Thr Ala Asn
245 250 255

His Ile His Ser Arg Lys Asp Thr
260

<210> 476
<211> 21
<212> PRT
<213> Homo sapiens

<400> 476
Asp Ile Met Pro Ala Ser Val Ile Phe Leu Ile Cys Glu Gly Val Leu
1 5 10 15

Tyr Gly Val Gln Gly
20

<210> 477
<211> 180
<212> PRT
<213> Homo sapiens

<400> 477
Gly Thr Ala Phe Gln His Ala Phe Ser Thr Asn Asp Cys Ser Arg Asn
1 5 10 15

Val Tyr Ile Lys Lys Asn Gly Phe Thr Leu His Arg Asn Pro Ile Ala
20 25 30

Gln Ser Thr Asp Gly Ala Arg Thr Lys Ile Gly Phe Ser Glu Gly Arg
35 40 45

His Ala Trp Glu Val Trp Trp Glu Gly Pro Leu Gly Thr Val Ala Val
50 55 60

Ile Gly Ile Ala Thr Lys Arg Ala Pro Met Gln Cys Gln Gly Tyr Val
65 70 75 80

Ala Leu Leu Gly Ser Asp Asp Gln Ser Trp Gly Trp Asn Leu Val Asp
85 90 95

Asn Asn Leu Leu His Asn Gly Glu Val Asn Gly Ser Phe Pro Gln Cys
100 105 110

Asn Asn Ala Pro Lys Tyr Gln Ile Gly Glu Arg Ile Arg Val Ile Leu
115 120 125

Asp Met Glu Asp Lys Thr Leu Ala Phe Glu Arg Gly Tyr Glu Phe Leu
130 135 140

Gly Val Ala Phe Arg Gly Leu Pro Lys Val Cys Leu Tyr Pro Ala Val
145 150 155 160

Ser Ala Val Tyr Gly Asn Thr Glu Val Thr Leu Val Tyr Leu Gly Lys
165 170 175

Pro Leu Asp Gly
180

<210> 478
<211> 35
<212> PRT
<213> Homo sapiens

<400> 478
Ala Arg Ala Phe Gln His Leu Met Val Ala Asp His Ser His Phe His
1 5 10 15

Arg Thr Leu Ile Lys Gln Pro Ser Met Ile Pro Asn Ala Thr Phe Tyr
20 25 30

His Ile Phe

35

<210> 479
<211> 131
<212> PRT
<213> Homo sapiens

<400> 479
Ala Arg Ala Leu Pro Glu Ile Lys Gly Ser Arg Leu Gln Glu Ile Asn
1 5 10 15

Asp Val Cys Ala Ile Cys Tyr His Glu Phe Thr Thr Ser Ala Arg Ile
20 25 30

Thr Pro Cys Asn His Tyr Phe His Ala Leu Cys Leu Arg Lys Trp Leu
35 40 45

Tyr Ile Gln Asp Thr Cys Pro Met Cys His Gln Lys Val Tyr Ile Glu
50 55 60

Asp Asp Ile Lys Asp Asn Ser Asn Val Ser Asn Asn Asn Gly Phe Ile
65 70 75 80

Pro Pro Asn Glu Thr Pro Glu Glu Ala Val Arg Glu Ala Ala Ala Glu
85 90 95

Ser Asp Arg Glu Leu Asn Glu Asp Asp Ser Thr Asp Cys Asp Asp Asp
100 105 110

Val Gln Arg Glu Arg Asn Gly Val Ile Gln His Thr Gly Ala Ala Ala
115 120 125

Gly Arg Ile
130

<210> 480
<211> 16
<212> PRT
<213> Homo sapiens

<400> 480
Phe Ser Thr Gln Ala Gln Gln Leu Glu Glu Phe Asn Asp Asp Thr Asp
1 5 10 15

<210> 481
<211> 22
<212> PRT
<213> Homo sapiens

<400> 481
Arg Leu Gln Glu Ile Asn Asp Val Cys Ala Ile Cys Tyr His Glu Phe
1 5 10 15

Thr Thr Ser Ala Arg Ile
20

<210> 482
<211> 20
<212> PRT
<213> Homo sapiens

<400> 482
Leu Tyr Ile Gln Asp Thr Cys Pro Met Cys His Gln Lys Val Tyr Ile
1 5 10 15

Glu Asp Asp Ile
20

<210> 483
<211> 21
<212> PRT
<213> Homo sapiens

<400> 483
Val Ser Asn Asn Asn Gly Phe Ile Pro Pro Asn Glu Thr Pro Glu Glu
1 5 10 15

Ala Val Arg Glu Ala
20

<210> 484
<211> 26
<212> PRT
<213> Homo sapiens

<400> 484
Asp Asp Ser Thr Asp Cys Asp Asp Asp Val Gln Arg Glu Arg Asn Gly
1 5 10 15

Val Ile Gln His Thr Gly Ala Ala Ala Gly
20 25

<210> 485
<211> 141
<212> PRT
<213> Homo sapiens

<220>
<221> SITE
<222> (54)
<223> Xaa equals any of the naturally occurring L-amino acids

<400> 485
Val Ala Gly Ile Thr Gly Ala His His His Ala Gln Leu Ile Phe Val
1 5 10 15

Leu Leu Val Glu Met Gly Phe His His Val Gly Gln Ala Gly Leu Lys
20 25 30

Leu Leu Thr Ser Asp Asn Pro Arg Thr Ser Ala Ser Gln Ser Ala Gly
35 40 45

Ile Thr Gly Met Ser Xaa Gly Arg Arg Ile Thr Cys Gly Gln Glu Phe
50 55 60

Lys Thr Ala Val Ser Tyr Asn Cys Thr Thr Ala Leu Gln Pro Asp Arg
65 70 75 80

Ala Lys Leu Cys Phe Leu Phe Lys Lys Lys Lys Lys Ile Ser Ile Gln
85 90 95

Arg Thr Leu Pro Gly Ile Lys Arg Val Ile Tyr Asn Tyr Glu Arg Val
100 105 110

Asp Ser Ser Lys Gly His Asn Ser Gln Val Gln Trp Ala His Ala Cys
115 120 125

Asn Pro Ser Thr Leu Gly Gly Arg Gly Gly Gln Ile Val
130 135 140

<210> 486
<211> 22
<212> PRT
<213> Homo sapiens

<400> 486
Ala Gly Ile Thr Gly Ala His His His Ala Gln Leu Ile Phe Val Leu
1 5 10 15

Leu Val Glu Met Gly Phe
20

<210> 487
<211> 27
<212> PRT
<213> Homo sapiens

<400> 487
Arg Val Ile Tyr Asn Tyr Glu Arg Val Asp Ser Ser Lys Gly His Asn
1 5 10 15

Ser Gln Val Gln Trp Ala His Ala Cys Asn Pro
20 25

<210> 488
<211> 106
<212> PRT
<213> Homo sapiens

<400> 488
Ala Gly Ala Glu Val Val Met Leu Phe Leu Leu Thr Pro Ser Ser His

```
 1               5                  10                  15

His Gln His Glu Cys Val Arg Arg Ala Phe Glu Cys Gly Asp Cys His
            20                  25                  30

Ile Leu Leu Asp Asn Asn Val Leu Gly Val Asp Cys His Gly Ala Gly
        35                  40                  45

Glu Arg Ala Val His Leu Glu Asp His Phe Val His Ile Asp Thr Ile
    50                  55                  60

Ser Leu Leu Leu Glu Asp Ala Leu Glu Tyr Ser Ala Leu Ile Ala Gly
65                  70                  75                  80

His Pro Lys Ser Asp Leu Pro Pro Gly Leu Ser Arg Cys Arg Pro Trp
                85                  90                  95

Glu His His Trp Pro Ile Ser Tyr Thr Gly
            100                 105
```

<210> 489
<211> 64
<212> PRT
<213> Homo sapiens

<400> 489

```
Thr Ile Ser Tyr Leu Cys Asn Asn Val Ser Tyr Met Gln Leu Gln Lys
 1               5                  10                  15

Leu Val Gly Lys Ser Met Ile Phe Leu Pro Tyr Ser Leu Pro Ile His
            20                  25                  30

Leu Pro Gly Asn His Arg Leu Leu Leu Pro Arg Val Gly Met Arg Leu
        35                  40                  45

Arg Gly Cys Cys Phe Ser Pro Tyr Ile Ile Thr Asp Phe Lys Trp Cys
    50                  55                  60
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<210> 490
<211> 58
<212> PRT
<213> Homo sapiens

<400> 490

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Glu Met Gly Gln Trp Cys Ser Gln Gly Leu His Leu Asp Ser Pro Gly
 1               5                  10                  15

Gly Lys Ser Asp Phe Gly Cys Pro Ala Ile Asn Ala Glu Tyr Ser Arg
            20                  25                  30

Ala Ser Ser Lys Ser Arg Leu Met Val Ser Met Trp Thr Lys Trp Ser
        35                  40                  45
```



```
Ser Arg Cys Thr Ala Leu Ser Pro Ala Pro
    50                  55
```

<210> 491
<211> 25
<212> PRT
<213> Homo sapiens

<400> 491

```
Arg Ala Phe Glu Cys Gly Asp Cys His Ile Leu Leu Asp Asn Asn Val
 1               5                  10                  15

Leu Gly Val Asp Cys His Gly Ala Gly
            20                  25
```

<210> 492
<211> 23
<212> PRT
<213> Homo sapiens

<400> 492

```
Leu Val Gly Lys Ser Met Ile Phe Leu Pro Tyr Ser Leu Pro Ile His
 1               5                  10                  15

Leu Pro Gly Asn His Arg Leu
            20
```

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13*bis*)

A. The indications made below relate to the microorganism referred to in the description on page 212, line N/A.

B. IDENTIFICATION OF DEPOSIT — Further deposits are identified on an additional sheet [X]

Name of depositary institution: American Type Culture Collection ("ATCC")

Address of depositary institution *(including postal code and country)*:
10801 University Boulevard
Manassas, Virginia 20110-2209
United States of America

Date of deposit	Accession Number
25 SEPTEMBER 1997	209229

C. ADDITIONAL INDICATIONS *(leave blank if not applicable)* — This information is continued on an additional sheet [ ]

DNA Plasmid No. PS062

In respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).

D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE *(if the indications are not for all designated States)*

E. SEPARATE FURNISHING OF INDICATIONS *(leave blank if not applicable)*

The indications listed below will be submitted to the International Bureau later *(specify the general nature of the indications e.g., "Accession Number of Deposit")*

For receiving Office use only	For International Bureau use only
[x] This sheet was received with the international application	[ ] This sheet was received by the International Bureau on:
Authorized officer: Sonya Barnes, PCT International Division SDB	Authorized officer

Form PCT/RO/134 (July 1992)

CANADA

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

NORWAY

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

AUSTRALIA

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

FINLAND

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

UNITED KINGDOM

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

Page 2

DENMARK

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later that at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

SWEDEN

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

NETHERLANDS

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

PCT/US98/22376

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13*bis*)

A. The indications made below relate to the microorganism referred to in the description on page 215, line N/A

B. IDENTIFICATION OF DEPOSIT Further deposits are identified on an additional sheet [X]

Name of depositary institution American Type Culture Collection

Address of depositary institution *(including postal code and country)*
10801 University Boulevard
Manassas, Virginia 20110-2209
United States of America

Date of deposit	Accession Number
25 SEPTEMBER 1997	209300

C. ADDITIONAL INDICATIONS *(leave blank if not applicable)* This information is continued on an additional sheet [ ]

DNA Plasmid No. PS063

In respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).

D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE *(if the indications are not for all designated States)*

E. SEPARATE FURNISHING OF INDICATIONS *(leave blank if not applicable)*

The indications listed below will be submitted to the International Bureau later *(specify the general nature of the indications e.g., "Accession Number of Deposit")*

For receiving Office use only	For International Bureau use only
[X] This sheet was received with the international application	[ ] This sheet was received by the International Bureau on:
Authorized officer Sonya Barnes PCT International Division SDB	Authorized officer

Form PCT/RO/134 (July 1992)

CANADA

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

NORWAY

The applicant hereby requests that the application has been laid open to public inspection (by the Norwegian Patent Office), or has been finally decided upon by the Norwegian Patent Office without having been laid open inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Norwegian Patent Office not later than at the time when the application is made available to the public under Sections 22 and 33(3) of the Norwegian Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on the list of recognized experts drawn up by the Norwegian Patent Office or any person approved by the applicant in the individual case.

AUSTRALIA

The applicant hereby gives notice that the furnishing of a sample of a microorganism shall only be effected prior to the grant of a patent, or prior to the lapsing, refusal or withdrawal of the application, to a person who is a skilled addressee without an interest in the invention (Regulation 3.25(3) of the Australian Patents Regulations).

FINLAND

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

UNITED KINGDOM

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

PCT/US98/22376

DENMARK

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later that at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

SWEDEN

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

NETHERLANDS

The applicant hereby requests that until the date of a grant of a Netherlands patent or until the date on which the application is refused or withdrawn or lapsed, the microorganism shall be made available as provided in the 31F(1) of the Patent Rules only by the issue of a sample to an expert. The request to this effect must be furnished by the applicant with the Netherlands Industrial Property Office before the date on which the application is made available to the public under Section 22C or Section 25 of the Patents Act of the Kingdom of the Netherlands, whichever of the two dates occurs earlier.

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13*bis*)

A. The indications made below relate to the microorganism referred to in the description on page 220, line N/A.

B. IDENTIFICATION OF DEPOSIT — Further deposits are identified on an additional sheet [X]

Name of depositary institution: American Type Culture Collection

Address of depositary institution *(including postal code and country)*:
10801 University Boulevard
Manassas, Virginia 20110-2209
United States of America

Date of deposit	Accession Number
02 OCTOBER 1997	209324

C. ADDITIONAL INDICATIONS *(leave blank if not applicable)* — This information is continued on an additional sheet [ ]

DNA Plasmid No. PS064

In respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).

D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE *(if the indications are not for all designated States)*

E. SEPARATE FURNISHING OF INDICATIONS *(leave blank if not applicable)*

The indications listed below will be submitted to the International Bureau later *(specify the general nature of the indications e.g., "Accession Number of Deposit")*

For receiving Office use only	For International Bureau use only
[X] This sheet was received with the international application	[ ] This sheet was received by the International Bureau on:
Authorized officer: Sonya Barnes, PCT International Division	Authorized officer

Form PCT/RO/134 (July 1992)

PCT/US98/22376

CANADA

The applicant requests that, until either a Canadian patent has been issued on the basis of an application or the application has been refused, or is abandoned and no longer subject to reinstatement, or is withdrawn, the Commissioner of Patents only authorizes the furnishing of a sample of the deposited biological material referred to in the application to an independent expert nominated by the Commissioner, the applicant must, by a written statement, inform the International Bureau accordingly before completion of technical preparations for publication of the international application.

NORWAY

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AUSTRALIA

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FINLAND

The applicant hereby requests that, until the application has been laid open to public inspection (by the National Board of Patents and Regulations), or has been finally decided upon by the National Board of Patents and Registration without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art.

UNITED KINGDOM

The applicant hereby requests that the furnishing of a sample of a microorganism shall only be made available to an expert. The request to this effect must be filed by the applicant with the International Bureau before the completion of the technical preparations for the international publication of the application.

Page 2

DENMARK

The applicant hereby requests that, until the application has been laid open to public inspection (by the Danish Patent Office), or has been finally decided upon by the Danish Patent office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the Danish Patent Office not later that at the time when the application is made available to the public under Sections 22 and 33(3) of the Danish Patents Act. If such a request has been filed by the applicant, any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Danish Patent Office or any person by the applicant in the individual case.

SWEDEN

The applicant hereby requests that, until the application has been laid open to public inspection (by the Swedish Patent Office), or has been finally decided upon by the Swedish Patent Office without having been laid open to public inspection, the furnishing of a sample shall only be effected to an expert in the art. The request to this effect shall be filed by the applicant with the International Bureau before the expiration of 16 months from the priority date (preferably on the Form PCT/RO/134 reproduced in annex Z of Volume I of the PCT Applicant's Guide). If such a request has been filed by the applicant any request made by a third party for the furnishing of a sample shall indicate the expert to be used. That expert may be any person entered on a list of recognized experts drawn up by the Swedish Patent Office or any person approved by a applicant in the individual case.

NETHERLANDS

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PCT/US98/22376

INDICATIONS RELATING TO A DEPOSITED MICROORGANISM

(PCT Rule 13*bis*)

A. The indications made below relate to the microorganism referred to in the description on page 225, line N/A.

B. IDENTIFICATION OF DEPOSIT — Further deposits are identified on an additional sheet ☐

Name of depositary institution: American Type Culture Collection ("ATCC")

Address of depositary institution *(including postal code and country)*:
10801 University Boulevard
Manassas, Virginia 20110-2209
United States of America

Date of deposit	Accession Number
09 OCTOBER 1997	209346

C. ADDITIONAL INDICATIONS *(leave blank if not applicable)* — This information is continued on an additional sheet ☐

DNA Plasmid No. PS065

In respect to those designations in which a European Patent is sought a sample of the deposited microorganism will be made available until the publication of the mention of the grant of the European patent or until the date on which application has been refused or withdrawn or is deemed to be withdrawn, only by the issue of such a sample to an expert nominated by the person requesting the sample (Rule 28 (4) EPC).

D. DESIGNATED STATES FOR WHICH INDICATIONS ARE MADE *(if the indications are not for all designated States)*

E. SEPARATE FURNISHING OF INDICATIONS *(leave blank if not applicable)*

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For receiving Office use only	For International Bureau use only
☑ This sheet was received with the international application	☐ This sheet was received by the International Bureau on:
Authorized officer: Sonya Barnes, PCT International Division SDB	Authorized officer

Form PCT/RO/134 (July 1992)

CANADA

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PCT/US98/22376

DENMARK

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/22376

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :Please See Extra Sheet.
US CL :Please See Extra Sheet.
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 536/23.5, 23.1; 435/320.1, 440, 252.3, 69.1, 7.1; 530/350, 387.1; 514/12

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Please See Extra Sheet.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	ADAMS et al. Complementary DNA sequencing: Expressed sequence tags and the human genome project. Science. 21 June 1991, Vol. 252, pages 1651-1656, see entire document.	1-22

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
13 JANUARY 1999	03 FEB 1999

Name and mailing address of the ISA/US	Authorized officer
Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	JAMES MARTINELL
Facsimile No. (703) 305-3230	Telephone No. (703) 308-0196

Form PCT/ISA/210 (second sheet)(July 1992)*

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/22376

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.: 23
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

Claim 23 is directed to a product of the process of claim 20. claim 20 is not a process for the production of a product, but a process for the detection of a substance. hence, no meaningful search can be carried out.

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

Form PCT/ISA/210 (continuation of first sheet(1))(July 1992)*

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/22376

A. CLASSIFICATION OF SUBJECT MATTER:
IPC (6):

G01N 33/68, 33/53; C07K 16/00; C12N 15/11, 15/12, 15/00, 15/63; A61K 38/17, 38/16; C12P 21/02

A. CLASSIFICATION OF SUBJECT MATTER:
US CL :

536/23.5, 23.1; 435/320.1, 440, 252.3, 69.1, 7.1; 530/350, 387.1; 514/12

B. FIELDS SEARCHED
Electronic data bases consulted (Name of data base and where practicable terms used):

APS, STN, MPSRCH (SEQ ID NOs 11 and 160 only). One nucleotide sequence and one amono acid sequence have been searched. It is not clear which sequences are embraced by the claims because the claims refer to sequences X and Y. The table beginning after page 209 contains many sequences X and Y, yet the claims refer to X and Y in the singular. If the claims are to embrace more than one X and more than one Y, it is not clear whether each X always requires the corresponding sequence Y. Additionally, the claims are in improper format in referring to the description (see PCT Rule 6.2(a)). Accordingly, the first X nucleotide sequence disclosed and the first Y amino acid sequence mentioned in the claims were searched.